ARCHIVES OF OPHTHALMOLOGY

VOLUME 36 (old series Volume 93) JULY 1946 NUMBER 1

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USE OF DIISOPROPYL FLUOROPHOSPHATE ("DFP") IN TREATMENT OF GLAUCOMA

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DIISOPROPYL fluorophosphate ("DFP") has been shown to have a marked and prolonged miotic effect in normal men and animals.[1] The miosis may be accompanied with spasm of accommodation and ciliary pain.[2] These effects have been shown to be due entirely to the inactivation of cholinesterase and not to direct action on the iris and ciliary muscle.[3] In this respect "DFP" is similar to physostigmine [4] and neostigmine,[5] but in its reaction with cholinesterase it is at least five and a half times as potent and much more persistent than physostigmine.[6] "DFP" can also overcome the effects of atropine and homatropine on the pupil and ciliary muscle.[3] Finally, "DFP" has been shown to resemble physostigmine in its influence on the intraocular tension of normal human eyes,[1h] differing, however, in that its effect is much more prolonged. Occasional normal human eyes show a rise in intraocular tension with "DFP," [1f, 1h] but the majority display a subnormal tension for several days after one local application of very dilute preparations of "DFP." [7]

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Physostigmine [8] and neostigmine [9] are also capable of producing elevated intraocular pressure in some normal eyes of animals and human subjects.

Because of the prolonged effect of very dilute preparations of "DFP" when locally applied to the normal eye, it seemed advisable to test the efficiency of this agent in glaucomatous eyes. Its lack of irritant properties had already been demonstrated in rabbits in which after application of a single lethal or repeated sublethal doses of "DFP" to the eyes there were no signs of clinically or histologically demonstrable damage to the eye,[1g] and even direct injections into the anterior chamber of 0.1 cc. of 0.1 per cent "DFP" produced no permanent ocular damage.[3] Studies of the pharmacologic action of "DFP" in the human subject by Comroe and co-workers [10] indicated that little if any danger of systemic toxicity would be encountered from doses considerably larger than those used locally in the eye.

Because of the necessity of using these drugs over long periods, it was essential to employ a stable preparation of "DFP." Koelle's [11] studies indicated that "DFP" was stable in peanut oil but not in aqueous solutions. Ten normal subjects were therefore tested for tolerance to fresh peanut oil (Planter's) by irrigating the eyes with 3 to 5 cc. of the oil twice daily for ten days. No subjective or objective signs of irritation were noted; the only effect was a slight blurring of vision for a few minutes following the instillation, due to the oily film.

The stability of solutions of "DFP" in oil and water was determined on normal rabbit eyes by the ability of these solutions to constrict the pupil. According to this test, a 0.1 per cent solution of "DFP" in peanut oil has maintained its potency for more than three months. The same concentration in water gradually lost its potency and was entirely without effect by the seventh day.[3]

In order to determine whether solutions of "DFP" in oil are as potent as aqueous solutions, 6 patients with normal pupillary phenomena were tested with 3 drops of 0.1 per cent "DFP" in oil in one eye and with 0.1 per cent "DFP" in water in the other eye. The pupils were measured in dim light. The eyes receiving "DFP" in water showed maximum constriction of the pupil a few minutes before those receiving "DFP" in oil, but the eventual degree and duration of effect on pupillary diameter and intraocular tension (which was significantly lowered for four to eight days) were the same in the two eyes.

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USE OF DIISOPROPYL FLUOROPHOSPHATE ("DFP") IN TREATMENT OF GLAUCOMA

METHOD

Fifty-two patients with glaucoma in one or both eyes were treated with "DFP" during a period of six months. These patients represent a total of 78 glaucomatous eyes. Whenever possible, intraocular tensions were measured throughout a preliminary twenty-four hour period, during which the patient received no miotic therapy. With almost all patients other miotic agents had been tried before "DFP" was used. All patients to be treated with "DFP" were admitted to the hospital for at least seventy-two hours, so that intraocular tensions could be watched throughout the entire period. Tensions were estimated with a Schiøtz tonometer, tetracaine hydrochloride (0.5 per cent) being used for topical anesthesia. Visual acuities and visual fields were tested, and ophthalmologic examinations were made weekly or biweekly on each patient. Gonioscopic examinations were made on those eyes in which miotic therapy failed. Only in the eyes in which tension was maintained at or below 30 mm. of mercury and in which no loss of visual fields occurred were the tensions considered controlled.

Solutions of 0.005 per cent "DFP" in oil failed significantly to lower intraocular tension in the first 3 eyes with chronic simple glaucoma in which it was tried. Subsequent clinical trial indicated that 0.05, 0.1 and 0.2 per cent concentrations in oil are suitable for use in such eyes. When a 0.2 per cent solution was ineffective, little was gained by using stronger concentrations.

RESULTS

The results are summarized in table 1. Certain comments should be made on these data. In 16 eyes of 13 patients [12] none of the miotics used (pilocarpine, physostigmine or "DFP") lowered the intraocular tension satisfactorily. The right eye of patient 45 proved on histologic study to have an intraocular growth, and that of patient 4 presented ophthalmoscopic evidence of an intraocular tumor but the patient refused to have enucleation. Patients 26, 34 and 42 had occlusion of the central retinal vein with secondary glaucoma and completely closed angles of the anterior chamber, according to gonioscopic examination. Patient 50 presented uveitis with secondary glaucoma and iris bombé following trauma. In patients 5, 37 (both eyes) and 38 (both eyes) the angles of the anterior chamber were too shallow for gonioscopic observation. The angles of the anterior chamber of patients 31 and 41 were only partly open. The left eye of patient 19 is also included in this series, as it responded partially, but not adequately, to treatment with "DFP" during a congestive phase.

12. Patient 4 (right eye), patient 5 (right eye), patient 19 (left eye), patient 26 (left eye), patient 28 (right eye), patient 31 (left eye), patient 34 (left eye), patient 37 (both eyes), patient 38 (both eyes), patient 41 (both eyes), patient 42 (right eye), patient 45 (right eye) and patient 50 (right eye).

TABLE 1.—*Comparison of Diisopropyl Fluorophosphate (DFP) and*

Patient	Eye	Age	Type of Glaucoma	Previous Operation	Visual Acuity with Correction	Tension Range Without Miotics (Schiøtz) Lowest, Mm. Hg	Tension Range Without Miotics (Schiøtz) Highest, Mm. Hg	Former Miotic Therapy
1. J. C.	O.D.	70	Glaucoma following cataract extraction	Combined intracapsular cataract extraction, both eyes (9/1939)	6/15	25	35	Pilocarpine, 1%, alone and with physostigmine 0.25%, 4 × daily
	O.S.				6/12	22	35	
2. H. R.	O.S.	65	Chronic simple glaucoma	Elliot trephination (9/1941) Elliot trephination (1/1944)	6/15	47	60	Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily
3. N. H.	O.D.	58	Glaucoma secondary to low grade uveitis	Combined cyclodialysis with iridectomy	6/22	28	35	Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily
	O.S.				6/12	28	41	
4. H. W.	O.D.	45	Intraocular tumor (not proved), uniocular glaucoma	None	Light perception	41	65	Pilocarpine, 1%, and physostigmine, 0.25%, 5 × daily
5. G. M.	O.D.	41	Uniocular chronic simple glaucoma—provocative test on left eye negative	None	6/60	35	40	Pilocarpine, 1%, and physostigmine, 0.25%, 6 × daily
6. M. S.	O.D.	45	Chronic simple glaucoma	None	6/9	25	40	Pilocarpine, 1%, 4 × daily
	O.S.				6/9	25	40	
7. T. H.	O.D.	59	Chronic simple glaucoma	None	6/15	35	40	Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily
8. R. R.	O.D.	60	Chronic simple glaucoma	Elliot trephination (1/1939) and 11/1939)	6/9	25	35	Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily
9. I. J.	O.D.	70	Glaucoma following cataract extraction	Extracapsular cataract extraction with iridectomy (5/1942)	6/15	25	35	Pilocarpine, 1%, 4 × daily
	O.S.			Intracapsular cataract extraction with iridectomy (2/1943), cyclodialysis (5/1943)	6/15	25	35	Pilocarpine, 1%, 4 × daily
10. E. B.	O.D.	61	Glaucoma following cataract extraction	Intracapsular cataract extraction with peripheral iridectomy (11/1944)	6/22	35	41	Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily
11. P. G.	O.S.	69	Chronic simple glaucoma	Elliot trephination (5/1944)	6/60	30	35	Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily
12. M. M.	O.S.	63	Chronic simple glaucoma	None	6/9	22	35	Pilocarpine, 1%, and physostigmine, 0.25%, 3 × daily
13. A. M.	O.D.	72	Chronic simple glaucoma	None	6/9†	25	41	Pilocarpine, 1%, and physostigmine, 0.25%, 3 × daily
	O.S.	..	Chronic simple glaucoma		6/9†	25	41	
14. V. F.	O.D.	53	Chronic simple glaucoma	Elliot trephination (1935)	Blind	35	40	Pilocarpine, 1%, and physostigmine, 0.25%, 4 × daily
	O.S.		Chronic simple glaucoma	Elliot trephination (1935)	6/9	30	35	
15. W. M.	O.S.	71	Post-cataract-extraction; iridocyclitis	Intracapsular cataract extraction with peripheral iridectomy	6/9	40	45	Physostigmine, 0.50%, 2 × hr.; no influence
16. E. M.	O.S.	66	Chronic simple glaucoma	None	6/9	22	30	Pilocarpine, 1%, t.i.
17. C. S.	O.D.	74	Chronic simple glaucoma	None	6/9	19	28	Pilocarpine, 0.5%, t.i.
	O.S.		Chronic simple glaucoma	None	6/12	19	28	
18. E. R.	O.D.	47	Acute primary glaucoma; duration twenty hours when patient first seen	None	Hand movements	4/10/45	45 at 5:30 p.m.	.....

* Pilocarpine nitrate and physostigmine salicylate were used. † Without correction.

Tension Range Former Therapy (Schiøtz)			Tension (Schiøtz) Range with "D F P" Therapy				
Lowest, Mm. Hg	Highest, Mm. Hg	"DFP" Therapy	Lowest, Mm. Hg	Highest, Mm. Hg	Visual Fields	Period of Observations	Comment
19	35	0.05% every 4 days	17	30	No significant change	6 mo.	No subjective symptoms
16	30		15	30			
35	41	0.05 or 0.1% 3 × daily	19	30	No significant change	5 mo.	No discomfort from drops, but patient discontinued drug for two weeks, with considerable loss of field
28	35	0.05 or 0.1% every	20	28	No significant change	6 mo.	Slight brow ache during first week of
28	41	3 to 4 days	19	25			therapy; none thereafter
41	65	0.05%, 1 instillation	No change over 2 hr. period		Not applicable	One day	Severe brow and eye ache
35	40	0.05%, 1 instillation	No change over 2 hr. period		Not applicable	One day	Severe brow and eye ache
19	25	0.05 or 0.1% every	13	22	No significant change	3 mo.	Severe brow and eye ache, blurring of
19	35	10 days; same every 4 days	13	26			vision, patient discontinued use of drops because of these symptoms
35	40	0.1% every 3 days	17	26	No significant change	6 mo.	No symptoms
					No significant change	6 mo.	Slight brow ache, considerable blurring of vision
19	35	0.1% every 2 days	16	28	No change	6 mo.	No discomfort
25	30	0.1% every 4 days	17	19	No change	6 mo.	No discomfort
25	30	0.1% every 4 days	17	19	No change	6 mo.	No discomfort
25	41	0.1% 2 × daily	19	22	No change	6 mo.	No discomfort
30	35	0.1% daily	23	30	No change	5 mo.	No discomfort
22	30	0.1% every 5 days	16	23	No change	5 mo.	Slight brow ache
25	41	0.1% every 3 days	15	25	No change	3 mo.	Severe eye and brow ache; patient discontinued drug because of these symptoms
25	41		11	20			
30	35	0.05%, 1 instillation	20	30	Blind; recent loss with	5 mo.	After each application visual blurring
21	35	every 3 days	15	30	pilocarpine and physostigmine; no further loss with "DFP"		for six hours, which does not prevent library work
40	40	0.1% "DFP";	32.5 in 20 min.		No loss on "DFP"	3 mo.	Slight brow ache for few hours after
		thereafter once	30 in 1 hr.				each instillation; drug discontinued;
		every 2 days	19	22			miotics no longer required
30	30	0.05%, 1 instillation every 5 days	16	22	No loss on "DFP"	3 mo.	Visual blurring for 3 hr., barely perceptible ciliary flush, no flare or floaters, brow ache on one occasion; patient preferred frequent instillations of pilocarpine to discomfort of "DFP"; so latter drug no longer used
23	23	0.05% every 4 days	16	25	Recent loss on use of	2 mo.	Visual blurring for 6-8 hr. after each
23			16	25	pilocarpine in both eyes; no further loss on "DFP"		instillation, fleeting ciliary flush, no flare or floaters; patient preferred frequent instillations of pilocarpine to discomfort of "DFP" so that drug was stopped
..	..	4/10/45: 0.1% at 5:30 p.m.	..	45	Iridectomy performed at 4 p.m. (4/11/45); no field loss evident on 4/20/45; vision, 4/20/45, 6/9 with correction; vision, 8/13/45, 6/9 with correction	4/10/45 (4 doses)	Some eye ache, but severe only on first instillation
		Repeated at 7:30 p.m.	..	35			
		Repeated at 9:30 p.m.	..	30			
		Repeated at 12 midnight		20			
		4/11/45: 6:00 a.m.	..	14			
		4:00 p.m.	..	14			

TABLE 1.—*Comparison of Diisopropyl Fluorophosphate ("DF*

Patient	Eye	Age	Type of Glaucoma	Previous Operation	Visual Acuity with Correction	Tension Range Without Miotics (Schiøtz) Lowest, Mm. Hg	Tension Range Without Miotics (Schiøtz) Highest, Mm. Hg	Former Miotic Therap
19. D. G.	O.D.	64	Chronic simple glaucoma	Acute exacerbation (3/1944), iridectomy (1944)	6/15	20	35	Pilocarpine, 1%, t. i. d.
	O.S.		Chronic simple glaucoma	None	6/12	19	30	Pilocarpine, 1%, t. i. d.
	O.S.		Acute exacerbation		Hand movements		45	Physostigmine, 0.5% every 15 min. for 1 h Physostigmine, 0.5 %, pilocarpine, 1%, ev hour for 4 hr. daily
20. A. R.	O.D.	54	Chronic simple glaucoma	None	6/12	22	28	Pilocarpine, 1%, 4 × da
	O.S.		Chronic simple glaucoma	Operation refused	1/60	40	50	Pilocarpine and phys tigmine, 0.25%, 4 × d
21. W. L.	O.D.	71	Chronic simple glaucoma	None	4/100	28	32	Pilocarpine, 1%, 3 × daily
	O.S.		Chronic simple glaucoma		6/12	25	35	Pilocarpine, 1%, 3 × daily
22. H. T.	O.D.	57	Glaucoma, post-cataract-extraction	Intracapsular cataract extraction (1937)	6/9	19	30	Pilocarpine, 1%, 4 × daily
	O.S.			Intracapsular cataract extraction (1938), cyclodialysis (11/1939), (7/1940)	6/60	19	35	Pilocarpine, 1%, 5 × daily
23. E. L.	O.D.	74	Chronic simple glaucoma	None	2/60 blind	25	35	Pilocarpine, 0.5%, 3
	O.S.		Chronic simple glaucoma	None	6/22-2 (?)	19	28	daily
24. S. F.	O.S.	53	Uveitis (Boeck's sarcoid), secondary glaucoma	Iridectomy (4/1945)	6/60	35	40	Physostigmine, 0.5% 4 × daily
25. A. W.	O.S.	65	Secondary glaucoma, iridocyclitis following capsulotomy	Extracapsular cataract extraction (5/1944), capsulotomy (3/1945)	6/100	55 (on atropine)	60	Physostigmine, 0.5% twice in 30 min.
26. E. T.	O.S.	70	Glaucoma secondary to occlusion of central retinal vein	None	Blind	76	..	Physostigmine, 0.2% every 15 min. for 1 h physostigmine, 0.25% pilocarpine, 1%, ev hour for 4 hr.
27. S. H.	O.S.	75	Glaucoma secondary to intracapsular cataract extraction	Intracapsular cataract extraction with peripheral iridectomy (6/1943), cyclodialysis (11/1943)	6/100	30	35	Physostigmine, 0.2% and pilocarpine, 1% 4 × daily
28. R. E.	O.D.	60	Absolute glaucoma	None	Blind	65	70	Physostigmine, 0.2%
	O.S.		Chronic simple glaucoma	Elliot trephination (5/1944), cyclodialysis (6/1944)	6/30†	25	35	and pilocarpine, 1% 4 × daily
29. B. H.	O.D.	41	Chronic congestive glaucoma	None	Blind	35	40	Physostigmine, 1% daily; pilocarpine, 0.
	O.S.		Chronic simple glaucoma	None	6/9	22	30	t. i. d.
30. R. P.	O.D.	55	Chronic simple glaucoma	Cyclodialysis (4/1940)	Blind	25	40	Pilocarpine, 1%, 4
	O.S.		Chronic simple glaucoma	Cyclodialysis (4/1940)	Light perception	25	35	daily or physostigm 0.25%, 4 × daily, gi alternately
31. E. B.	O.D.	74	Chronic simple glaucoma	None	6/12	30	40	Physostigmine, 1%, 4
	O.S.		Chronic simple glaucoma	None	6/9	35	47	daily

* Pilocarpine nitrate and physostigmine salicylate were used. † Without correction.

Tension Range Former Therapy (Schiøtz)			Tension (Schiøtz) Range with "D F P" Therapy				
Lowest, Mm. Hg	Highest, Mm. Hg	"DFP" Therapy	Lowest, Mm. Hg	Highest, Mm. Hg	Visual Field	Period of Observations	Comment
30	35	0.05% 2 × daily	16	25	No loss of field on use of "DFP" or of pilocarpine	4½ mo.	No discomfort; eye ache with each instillation
30	30	0.1% "DFP," 1 instillation	..	40			
		1 hr. later	..	30			
40	..	4 hr. later	..	19			
		12 hr. later	..	13			
40	..	20 hr. later	..	35			
		"DFP" repeated	..	35			
		1 hr. later, pilocarpine and physostigmine	..	35			
		1 hr. later	..	35			
		Iridectomy performed	..	35			
		Tension since without miotic therapy	..	16			
27	28		19	22	No loss	4½ mo.	Blurred vision for 1-2 hr. after each instillation
30	50	0.05% once daily	19	28			
22	28	0.05% once every 3 days	19	25	No loss	4½ mo.	Blurred vision for 6 hr. after each instillation
22	28		19	28			
19	25	0.05% once every 7 days	16	22	No loss	3 mo.	On first instillation, marked ciliary flush, no flare or floaters in anterior chamber; flush not noted with subsequent instillations; patient bothered by redness of eyes and was greatly concerned with effects; drug was therefore stopped
19	28	0.05% once every 5 days	16	25			
21	35	0.05% once daily	16	30	Recent loss with pilocarpine, no further loss with "DFP"	4½ mo.	Blurring and some brow ache for 4 hr. after each instillation
19	25		13	22			
30	40	0.05% once daily, use discontinued after 4 days, with clearing of hemorrhage in anterior chamber; tension subsided spontaneously	22	30	.....	4 days	Eye ache, quite severe for 1-2 hr. after each instillation
No benefit; after 1½ hr.	55	0.05% 3 × daily in first 24 hr. and thereafter once daily; benefit after first instillation apparent in 15 min.	20	25	No loss with "DFP," iridocyclitis not subsided	1 mo.	Slight eye ache on initial doses, not with subsequent ones; drug discontinued after 1 mo.; cyclodialysis performed
	76	0.1% every 2 hr. for 8 hr.		76	Fields subsequently reduced with iridencleisis	8 hr.	Eye ache similar to that with physostigmine, perhaps slightly more severe
	35	0.05% once daily	20	26	No loss with "DFP"	4½ mo.	Eye ache for 1 hr. with first 2 instillations; much less with subsequent instillations; in last month no discomfort
	75	0.05% once daily	40	48	Blind	2½ mo.	Some blurring of vision in left eye, no ache; but some ache in (blind) right eye, not noted on recent instillations; patient greatly concerned by blurred vision in left eye; visual field only 5 degrees about fixation, so that drug was discontinued
	30		22	30	No loss with "DFP"		
	40	Tension initially lowered with 0.05%	13	16	Blind	2½ mo.	Ache in brow and eye on first day,
	25	"DFP" 4 × in 24 hr. then 0.05% once daily, 0.05% once every 7 days	13	19	No loss with "DFP"	4½ mo.	visual blurring for 3 hr. after each instillation; right eye enucleated after 2½ mo. for cosmetic purposes
	35	0.05% once daily	25	30	Blind	3½ mo.	No discomfort; patient uncooperative, so the drug was discontinued after 3½ mo. trial
	30		22	30	No further loss		
	35	0.05% twice daily	19	25	No loss	4/16/45 to 6/2/45	Ciliary injection and slight blurring in both eyes; conjunctival folliculosis from use of physostigmine cleared. O.D.: Elliot trephination (6/2/45); patient disliked brow and eye ache and visual blurring in this eye. O.S.: Elliot trephination (4/27/45)
	47		25	35	No loss	4/16/45 to 4/27/45	

TABLE 1.—*Comparison of Diisopropyl Fluorophosphate ("DF*

Patient	Eye	Age	Type of Glaucoma	Previous Operation	Visual Acuity with Correction	Tension Range Without Miotics (Schiøtz) Lowest, Mm. Hg	Tension Range Without Miotics (Schiøtz) Highest, Mm. Hg	Former Miotic Therapy
32. M. S.	O.S.	65	Chronic simple glaucoma	None	Light perception	26	30	Pilocarpine, 1%, t.i.
33. A. B.	O.D.	64	Chronic simple glaucoma	None	6/12	28	35	Pilocarpine, 1%, 4 ×
	O.S.		Chronic simple glaucoma	None	6/15-1	28	35	daily
34. W. D.	O.S.	72	Postvenous occlusion	None	Blind	55	60	Pilocarpine, 1%, and physostigmine, 0.5%, 5 × daily
35. J. B.	O.D.	58	Absolute glaucoma	None	Blind	40	45	Pilocarpine, 1%, and
	O.S.		Chronic simple glaucoma	None	6/12	30	40	physostigmine, 0.25%, 4 × daily
36. J. D.	O.D.	53	Chronic simple glaucoma	None	4/60	30	35	Pilocarpine, 1%, 5 ×
	O.S.		Chronic simple glaucoma	None	3/60	25	38	daily
37. W. D.	O.D.	48	Chronic congestive glaucoma	None	6/9	40	58	Pilocarpine, 1%, and physostigmine, 0.5%
	O.S.		Chronic congestive glaucoma	None	Hand movements	40	61	1%, 5 × daily
	O.D.		Chronic congestive glaucoma	Basal iridectomy (5/22/45)	6/60†	30	38	Pilocarpine, 1%, and physostigmine, 0.5%, 4 × daily
38. S. W.	O.D.	50	Chronic congestive glaucoma	None	6/9	30	40	Pilocarpine, 1%, and physostigmine, 0.5%
	O.S.		Chronic congestive glaucoma	None	Blind	45	51	5 × daily
39. J. L.	O.D.	48	Chronic simple glaucoma	Elliot trephination (1/1945)	6/9	60	35	Physostigmine, 2%
	O.S.		Chronic simple glaucoma	Cyclodialysis (3/1945)	6/15	30	40	4 × daily
40. E. F.	O.D.	58	Glaucoma secondary to exfoliating lens capsule	Elliot trephination (10/1944)	6/30	30	40	Pilocarpine, 1%, 5 × daily
41. J. H.	O.D.	39	Chronic simple glaucoma	None	6/7.5	45	56	Pilocarpine, 1%, and
	O.S.		Chronic simple glaucoma	None	Hand movements	50	61	physostigmine, 0.25%, 4 × daily
42. J. W.	O.D.	65	Postvenous occlusion	None	Blind	40	58	Physostigmine, 0.5% pilocarpine, 1%, 4 × daily
43. S. N.	O.D.	67	Chronic simple glaucoma	Iridectomy (3/25/44)	6/12	25	40	Pilocarpine, 2%, 5 × daily
44. P. D.	O.D.	64	Chronic simple glaucoma	Elliot trephination (10/1944)	6/6-1	30	40	Pilocarpine, 1%, and physostigmine, 0.25%, 5 × daily
45. J. S.	O.D.	65	Glaucoma secondary to intraocular growth	None	Light perception	50	60	Physostigmine, 0.5% pilocarpine, 1%, 4 × daily
46. F. M.	O.S.	56	Secondary to uveitis	None	6/20	40	45	No miotics, tried, atropine, 1%, 2 ×
47. J. G.	O.S.	46	Chronic simple glaucoma	None	6/22	27	41	Pilocarpine, 1%, and physostigmine, 0.5%, 4 × daily
48. B. A.	O.D.	74	Chronic simple glaucoma	None	6/15	30	40	Pilocarpine, 1%, and
	O.S.		Chronic simple glaucoma	None	Light perception	30	47	physostigmine, 0.5%, 4 × daily
49. L. S.	O.D.	55	Chronic simple glaucoma	None	6/9	26	35	Pilocarpine, 1%, and
	O.S.		Chronic simple glaucoma	None	6/20	30	36	physostigmine, 0.5%, 5 × daily
50. B. T.	O.D.	35	Traumatic uveitis, secondary glaucoma, iris bombé	None	Light perception	40	45	Pilocarpine, 1%, and physostigmine, 0.5%, 4 × daily
51. R. L.	O.D.	60	Chronic simple glaucoma	None	6/22†	35	47	Pilocarpine, 1%, 5 ×
	O.S.		Chronic simple glaucoma	None	6/22†	30	47	daily
52. M. H.	O.D.	45	Secondary glaucoma; trauma many years previously, aggravated by recent trauma; hemorrhage of anterior chamber	None	Light perception	67	67	Physostigmine, 0.5% hourly for 10 hr.
						On first visit within 1 hr.		

* Pilocarpine nitrate and physostigmine salicylate were used. † Without correction.

Tension Range Former Therapy (Schiøtz)			Tension (Schiøtz) Range with "D F P" Therapy				
Lowest, Mm. Hg	Highest, Mm. Hg	"DFP" Therapy	Lowest, Mm. Hg	Highest, Mm. Hg	Visual Field	Period of Observations	Comment
22	26	0.05% once every third day	13	20	No loss	4 mo.	Slight ciliary injection; no flare or floaters in aqueous
19	30	0.05% every 4 days	13	22	Slight loss in field	4 mo.	Slight blurring in both eyes; slight ciliary flush in first weeks of treatment; ciliary flush in past 2 mo.
19	28		13	22			
55	60	0.1% 4 × daily	40	50	Blind	10 days	No discomfort from "DFP," iridencleisis performed on left eye, with satisfactory lowering of tension and clearing of epithelial blebs
40	45	0.1% twice daily	22	30	Blind eye	14 days	Considerable blurring of vision; this alarmed patient, so that he desired to return to use of old drops (pilocarpine and physostigmine); has only 5 degree field about fixation in left eye
22	35	0.1% once daily	13	22	No change with "DFP"		
22	30	0.1% once every	13	22	No change with "DFP"	21 days	Considerable eye ache and blurring of vision; patient returned to use of pilocarpine
25	30	5 days	13	19			
35	50	0.1%, 3 × daily	30	50	No change with "DFP"	4 days	Discomfort similar to that of pilocarpine and physostigmine, same eye ache; iridencleisis, left eye; iridectomy, right eye, with satisfactory control of tension in left eye
40	61	0.1% 3 × daily	35	58			
28	35	0.1% 3 × daily	28	32	No further loss	2 mo.	
30	35	0.1% 3 × daily	30	35	No change with "DFP"	4 days	Severe ache in each eye; drug discontinued; iridencleisis, right eye; enucleation, left eye
45	51		45	51			
20	28	0.1% 2 × daily	20	28	No change with "DFP"	10 days	No discomfort from either physostigmine or M. G.; return to physostigmine because patient could not be followed adequately
20	25		20	28			
30	35	0.05% once every 5 days	17	23	No change with "DFP"	4 mo.	No discomfort
22	47	0.1%, 2 × daily	25	47	No change with "DFP"	5 days	Eye ache, blurring of distant vision; no improvement over that with physostigmine and pilocarpine; Elliott trephination on both eyes
22	45	0.1% 2 × daily	22	40			
40	48	0.1% 3 × daily	40	50	Blind	3 days	No discomfort
25	35	0.05% once every 4 days	16	22	Not reliable	3½ mo.	Slight eye ache for 1-2 hr. after each instillation during first 2 wk. of treatment; no symptoms during last 2 mo.
30	35	0.05% 2 × daily	23	28	No change with "DFP"	3 mo.	Considerable blurring of distant vision; eye ache
30	60	0.1%, one application in 24 hr.	50	60	.....	Trial for only 1 day	Severe ocular pain following instillation, duration several hours
45	47	0.1% 2 × daily	13	19	No loss	3 wk.	Had only 2 applications of "DFP"; uveitis subsequently quieted
35	41	0.1% once daily	19	25	No further loss	2 mo.	Some blurring of distant vision, slight ache for 30 min.; patient in mental institution for 4 days without ocular treatment, after which he showed significant loss of field
27	35	0.1% once daily	16	23	No further loss	6 wk.	Blurred vision; patient quite bothered by it
30	40		16	25			
30	35	0.1% once every	13	19	No further loss	2 mo.	Eye ache, duration 1-2 hr.; slightly blurred vision
28	32.5	third day	13	26			
40	45	0.1% 3 × daily	40	45	Not under treatment with "DFP" long enough	Tried only 1 day	Transfixion successfully lowered tension
41	47	0.1% once daily	26	30	No further loss	2 mo.	Brow ache; circumcorneal injection in both eyes for first six days of treatment, none since
35	41		16	22			
57	67	0.1% "DFP" 3 × in 24 hr., stopped in 48 hr.	22	30	Not under treatment with "DFP" long enough	1 mo.	Paracentesis performed and anterior chamber cleared of hemorrhage after tension lowered by "DFP," use of "DFP" discontinued thereafter

In 24 eyes of 17 patients [13] pilocarpine, physostigmine or a combination of the two lowered intraocular tension to or below 30 mm. of mercury. In all these eyes "DFP" lowered intraocular tension to the same or (usually) a lower level.

In 36 eyes of 29 patients [14] pilocarpine, physostigmine or a combination of the two failed to reduce the intraocular tension to within normal limits and to prevent further loss of visual fields. In each of these eyes "DFP" succeeded in lowering and maintaining the intraocular tension to or below 30 mm. of mercury and prevented further loss of visual fields during the period of observation.

In 2 eyes (patient 18, right eye, and patient 46, left eye) no miotics other than "DFP" were tried. In both eyes "DFP" successfully lowered the intraocular tension. Patient 18 suffered an attack of acute primary glaucoma of the right eye, and a basal iridectomy was performed after the intraocular tension had been lowered. Patient 46 exhibited glaucoma secondary to uveitis, which subsequently subsided when the acute exacerbation of increased intraocular tension was controlled with "DFP."

In all the 60 eyes in which "DFP" successfully reduced the intraocular tension and in which pilocarpine and physostigmine were also tried, the duration of action of "DFP" greatly exceeded that of pilocarpine and/or physostigmine. The latter drugs were required at least three times a day and in many instances four, five or six times daily. "DFP," however, was required as often as three times daily in only 3 eyes [15]; twice daily in 7 eyes [16]; once daily in 17 eyes [17]; once every

13. Patient 1 (table 1) (left eye), patient 6 (right eye), patient 9 (both eyes), patient 12 (left eye), patient 16 (left eye), patient 17 (both eyes), patient 20 (right eye), patient 21 (both eyes), patient 22 (both eyes), patient 23 (left eye), patient 28 (left eye), patient 29 (left eye), patient 30 (left eye), patient 32 (left eye), patient 33 (both eyes), patient 36 (both eyes) and patient 39 (both eyes).

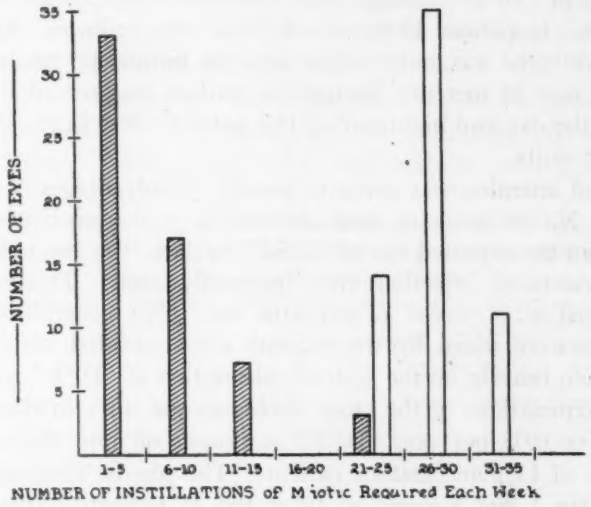
14. Patient 1 (right eye), patient 2 (left eye), patient 3 (both eyes), patient 6 (left eye), patient 7 (right eye), patient 8 (right eye), patient 10 (right eye), patient 11 (left eye), patient 13 (both eyes), patient 14 (both eyes), patient 15 (left eye), patient 19 (right eye), patient 20 (left eye), patient 23 (right eye), patient 24 (left eye), patient 25 (left eye), patient 27 (left eye), patient 29 (right eye), patient 30 (right eye), patient 31 (both eyes), patient 35 (both eyes), patient 40 (right eye), patient 43 (right eye), patient 44 (right eye), patient 47 (left eye), patient 48 (right eye), patient 49 (both eyes), patient 51 (both eyes) and patient 52 (right eye).

15. Patient 2 (left eye), patient 52 (both eyes).

16. Patient 10 (right eye), patient 19 (right eye), patient 31 (right eye), patient 35 (right eye), patient 49 (both eyes) and patient 44 (right eye).

17. Patient 11 (left eye), patient 20 (both eyes), patient 23 (both eyes), patient 24 (left eye), patient 25 (left eye), patient 28 (left eye), patient 29 (right eye), patient 30 (both eyes), patient 35 (left eye), patient 47 (left eye), patient 48 (right eye) and patient 51 (both eyes).

second day in 2 eyes[18]; once every third day in 12 eyes[19]; once every fourth day in 10 eyes[20]; once every five days in 6 eyes[21]; once every seven days in 2 eyes,[22] and once every ten days in 1 eye.[23] These observations are summarized in the graph which shows clearly that the frequency of application of "DFP" was decidedly less than that required with pilocarpine and/or physostigmine.



Comparison of frequency of instillations required for the maintenance of intraocular tension in glaucomatous eyes using pilocarpine nitrate, 1 per cent, and/or physostigmine salicylate, 0.2-0.5 per cent, and using diisopropyl fluorophosphate ("DFP") 0.05-0.1 per cent.

The hatched rectangles indicate values for the eyes treated with "DFP"; the clear rectangles, values for eyes treated with pilocarpine and/or physostigmine.

In the several instances in which the patient was returned to pilocarpine or physostigmine therapy after a trial of "DFP" no improvement in the effectiveness of the former drugs could be noted.[24] In this

18. Patient 8 (right eye), patient 15 (left eye).

19. Patient 3 (both eyes), patient 7 (right eye), patient 14 (both eyes), patient 21 (both eyes), patient 32 (left eye), patient 49 (both eyes), patient 13 (both eyes).

20. Patient 1 (both eyes), patient 6 (left eye), patient 9 (both eyes), patient 17 (both eyes), patient 33 (both eyes), patient 43 (right eye).

21. Patient 12 (left eye), patient 16 (left eye), patient 22 (left eye), patient 36 (both eyes) and patient 40 (right eye).

22. Patient 22 (right eye), patient 29 (left eye).

23. Patient 6 (right eye).

24. Patient 6 (both eyes), patient 13 (both eyes), patient 16 (left eye), patient 17 (both eyes), patient 22 (both eyes), patient 28 (both eyes), patient 35 (both eyes), patient 36 (both eyes) and patient 39 (both eyes).

respect "DFP" was unlike carbaminoylcholine chloride, which Clarke [25] found to enhance the effects of the two miotic alkaloids.

Of all the 60 eyes in which the intraocular tension was maintained below 30 mm. of mercury with "DFP" in only 2 (patient 33, both eyes) were slight but significant losses of the visual fields encountered. All other eyes retained the visual fields that they had possessed at the beginning of "DFP" therapy. The duration of observation is recorded in table 1. In patient 33 the visual fields were reduced. However, at no time while she was under therapy was the intraocular tension recorded above 22 mm. of mercury, though the tension was recorded at various hours of the day and night during this patient's stay in the hospital and her clinic visits.

Careful attention was given to possible disadvantages of this miotic therapy. No evidence of local dermatitis or conjunctivitis has been noted from the repeated use of "DFP" to date. On the initial instillations pericorneal injection was frequently seen. This was rarely encountered after weeks of constant use.[3] No generalized systemic symptoms were noted by the patients after repeated use of "DFP." Information bearing on the systemic absorption of "DFP" was obtained from determinations of the blood cholinesterase after instillation of 0.1 per cent or 0.05 per cent "DFP" in peanut oil into the conjunctival cul-de-sac of 11 glaucomatous patients. The plasma cholinesterase was increased in 1 and lowered in 10 of the 11 patients. Five of the 10 patients showed a reduction of 10 per cent or less; the maximum decrease was 29 per cent. The cholinesterase content of the red blood cells showed no consistent changes in the 11 subjects. The second sample of blood was obtained one hour (1 patient), one and one-half hours (5 patients) and five hours (1 patient) after the instillation of "DFP" in both eyes. These changes, when compared with the daily fluctuations in normal persons, indicate either that no systemic absorption had occurred or that the amounts absorbed were too small to produce any significant general symptoms.[3]

Many of the patients complained of severe headache, brow ache, or a drawing or pulling eye ache after instillation of 0.05 or 0.1 per cent "DFP" (table 1). This sensation persisted for varying lengths of time. In addition, the majority of the patients were bothered with visual blurring, which was undoubtedly due to the ciliary spasm. Frequently these symptoms appeared only on attempted close work. Similar symptoms have been noted in normal eyes after instillation of "DFP."[26] Near point measurements and manifest refractions revealed that spasm

25. Clarke, S. T.: The Use of Doryl in the Treatment of Glaucoma, Am. J. Ophth. **25**:309, 1942.

26. Cullumbine.[1f] Scholz and Wallen.[1h] Leopold and Comroe.[3]

of accommodation was responsible. The false myopia was greatest within the first few hours after instillations of "DFP" and lessened gradually. As a result, it was not possible to prescribe an optical correction which would be satisfactory at all times. There was slight but insignificant lessening of the ciliary spasm with repeated use of the drug.

Nine of the patients, representing 17 glaucomatous eyes, were so bothered by one or more of these symptoms that they asked to be returned to their previous medication.[27]

Summary.—Seventy-eight glaucomatous eyes of 52 patients were treated with "DFP." A summary of the results is given in table 2. It is evident that of the eyes with chronic simple glaucoma,

TABLE 2.—*Comparison of Results of Treatment of Eyes with Various Types of Glaucoma Using Pilocarpine and/or Physostigmine and Using Diisopropyl Fluorophosphate ("DFP")*

Type of Glaucoma	No. of Eyes	Eyes Treated with Pilocarpine and/or Physostigmine		Eyes Treated with "D F P"	
		Tension Controlled	Tension Uncontrolled	Tension Controlled	Tension Uncontrolled
Acute primary	1	Not tried		1	0
Chronic congestive	5	0	5	1	4
Chronic simple	48	21	27	43	5
Absolute	2	0	2	1	1
Glaucoma with exfoliating lens capsule	1	0	1	1	0
Glaucoma following occlusion of central retinal vein	3	0	3	0	3
Glaucoma secondary to intraocular growth	2	0	2	0	2
Glaucoma after cataract extraction	10	4	6	10	0
Glaucoma secondary to uveitis	6	0	5	5	1
Totals	78	25	51	62	16

pilocarpine and/or physostigmine was successful in controlling the intraocular tension in only 43.7 per cent. Of the same eyes, "DFP" was successful in keeping the tension below 30 mm. of mercury in 89.5 per cent. Of eyes in which glaucoma developed after cataract extraction, pilocarpine and/or physostigmine was successful in lowering an intraocular tension below 30 mm. of mercury in only 40 per cent, whereas "DFP" was successful in 100 per cent. It is interesting to note the greater effect of "DFP" in controlling the intraocular tension in the few eyes with glaucoma secondary to uveitis, but great significance cannot be attached to this small series. The great variability in the tension curve of eyes with glaucoma secondary to uveitis has

27. Patient 6 (both eyes), patient 13 (both eyes), patient 16 (left eye), patient 17 (both eyes), patient 22 (both eyes), patient 28 (both eyes), patient 35 (both eyes), patient 36 (both eyes) and patient 39 (both eyes).

been noted by Kronfeld.[28] It is possible that "DFP" therapy was started in a relatively favorable interval.

RECOMMENDED THERAPY WITH "DFP" IN CASES OF GLAUCOMA

Experience with "DFP" has not been great enough to allow one to stipulate the exact method of administration in each case of glaucoma. However, the drug should not be ordered to be used empirically three times, or even once, a day. The frequency of application can be determined only by repeated checks of the intraocular tension throughout the first twenty-four hours and daily thereafter. As in the cases presented here, administration may be required only once daily, or even once weekly. The visual fields must be closely observed.

COMMENT

In the past decade several new drugs have been introduced into ophthalmology as therapeutic agents for glaucoma, namely, mecholyl and neostigmine,[29] carbaminoylcholine chloride [30] and furfuryl trimethyl ammonium iodide (Furmethide).[31] Of these, neostigmine is the only anticholinesterase agent. None of these drugs has proved to be the answer to treatment of all forms of glaucoma, but each has a definite place and value in the therapy of this condition. "DFP," an anticholinesterase agent with a much more prolonged action than either neostigmine or physostigmine, also does not fulfil all the requirements of an ideal miotic antiglaucomatous agent, but it has certain attributes which entitle it to serious consideration.

In the first place, it is very effective. We have shown that "DFP" in concentrations of 0.05 to 0.1 per cent in oil will lower intraocular

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28. Kronfeld, P. C.: Gonioscopic Correlates of Responsiveness to Miotics, Arch. Ophth. **32**:447 (Dec.) 1944.

29. Kull.[9] Montalvan, P.: Prostigmin in the Treatment of Glaucoma, Am. J. Ophth. **26**: 57, 1943. Clarke, S. T.: Mecholyl and Prostigmin in the Treatment of Glaucoma, ibid. **22**:249, 1938. Gifford, S. R.: Treatment of Secondary Glaucoma, Arch. Ophth. **23**:301 (Feb.) 1940. Johnson, L. V.: Newer Concepts in the Treatment of Glaucoma, Ohio State M. J. **37**:36, 1941.

30. Clarke.[25] Velhagen, K., Jr.: Action of Choline Bodies on Muscles of Iris: Double Innervation, Arch. f. Augenh. **108**:126, 1933; Practical Use of Carbaminoylcholine, Klin. Monatsbl. f. Augenh. **92**:472, 1934. Wilenkin, M.: Effect of Carbaminoylcholine on Intraocular Pressure and on Width of Pupil, ibid. **96**: 84, 1936. O'Brien, C. S., and Swan, K. C.: Carbaminoylcholine Chloride in the Treatment of Glaucoma Simplex, Arch. Ophth. **27**:253 (Feb.) 1942. Myerson, A., and Thau, W.: Effect of Cholinergic and Adrenergic Drugs upon the Eye, ibid. **18**:78 (July) 1937. Hardesty, J. F.: The Use of Doryl in Glaucoma, Am. J. Ophth. **27**:623, 1944.

31. Myerson, A., and Thau, W.: Ocular Pharmacology of Furfuryl Trimethyl Ammonium Iodide, Arch. Ophth. **24**:758 (Oct.) 1940. Uhler, E. M.: The Use of Furmethide in Comparison with Other Miotics for the Treatment of Glaucoma, Am. J. Ophth. **26**:710, 1943.

tension even in glaucomatous eyes not satisfactorily maintained with aqueous solutions of 1 per cent pilocarpine nitrate or 0.25 to 0.5 per cent physostigmine salicylate. Another outstanding feature of this agent is the infrequency of application required. It is interesting to note that although 0.05 per cent "DFP" or weaker solutions in water or oil produced miosis which lasted one to two weeks on the average in normal human eyes, the duration of the miosis in glaucomatous eyes was much less than this. The longest miotic effect in any glaucomatous eye was twelve days, in patient 6 (right eye), and the shortest was twelve hours, in patient 2 (left eye). These observations suggest that there may be some fundamental derangement in the acetylcholine-cholinesterase system in glaucoma.

Six months may be an insufficient period in which to evaluate this therapy, and the value of "DFP" in long term therapy must still be determined. However, its proficiency in reducing intraocular tension over a period of months appears to be established by these data. It should also be borne in mind that the prolonged action of "DFP" may further be beneficial in reducing the fluctuations in tension that occur over each twenty-four hour period and thus in reducing the destructive effect of labile elevated ocular tension.

Although it is true that this agent does have certain disadvantages that preclude its universal use in antiglaucoma therapy, there are patients in whom the untoward effects are not troublesome and in whom in spite of these untoward effects "DFP" may prove to be of considerable value. Some of these uses may be indicated: 1. "DFP" produces little discomfort in patients with glaucomatous, aphakic eyes, and it appears to be a most effective agent in controlling the tension in such eyes.[32] 2. "DFP" is able to overcome the pupillary and accommodative effects of atropine and should prove of therapeutic value in preglaucomatous and glaucomatous eyes unfortunately and inadvertently treated with atropine. 3. "DFP" may be helpful in controlling the tension in eyes in which operation must be postponed and pilocarpine or physostigmine has proved ineffective. 4. "DFP" may properly be used initially in relief of acute congestive glaucoma, since

32. This action is difficult to explain. The ciliary muscle is intact in the aphakic eye, as in the eye with a lens, but the zonule fibers are relaxed and have no firm insertion in the aphakic eye. This suggests that intact zonule fibers must be present for the pain of ciliary spasm to develop. If this is so, one would expect ciliary pain when the zonule fibers are stretched. According to the Helmholtz theory of accommodation, these fibers are relaxed when the ciliary muscle is contracted. The Tscherning theory teaches that the zonule fibers are stretched during spasm of the ciliary muscle. The latter theory would explain the decidedly less degree of discomfort in the aphakic eye after instillation of "DFP" than in the intact eye, since in the aphakic eye the zonule fibers cannot be stretched.

it is a more powerful agent than physostigmine. In other words, this anticholinesterase agent can be used in eyes in which physostigmine formerly was employed.

SUMMARY

Diisopropyl fluorophosphate ("DFP") is an anticholinesterase agent capable of producing prolonged and marked parasympathomimetic effects in the eye.

"DFP" has successfully lowered intraocular tension in glaucomatous eyes in 0.05 or 0.1 per cent concentration in a peanut oil vehicle.

In the majority of the glaucomatous eyes treated with 0.05 or 0.1 per cent oily solutions of "DFP" the intraocular tension was controlled with decidedly fewer daily instillations than when either 1 per cent pilocarpine nitrate and/or 0.25 to 0.5 per cent physostigmine salicylate in water was employed.

In all glaucomatous eyes successfully treated with pilocarpine or physostigmine "DFP" was also effective and usually maintained the intraocular pressure at a lower level.

No instance of dermatitis or conjunctivitis due to repetitive use of "DFP" was encountered in the 78 eyes tested.

In 36 of the 78 glaucomatous eyes in which treatment with pilocarpine or physostigmine had previously failed, "DFP" succeeded in maintaining intraocular tension below 30 mm. of mercury.

"DFP" has several untoward and undesirable ocular effects, namely, visual blurring, brow ache and eye ache, spasm of accommodation and pericorneal injection.

A slight depressant effect on serum cholinesterase could be detected from ocular instillations of "DFP" in a few cases, but no systemic symptoms were elicited by ocular administration in any of the 52 patients treated.

The special usefulness of this drug in ophthalmology is discussed.

NOTE.—Among the eyes treated with "DFP" since this paper was submitted there have been 2 which have shown a rise in intraocular tension after the instillation of "DFP." One of these eyes had chronic simple glaucoma and the other congenital glaucoma. The tension in the congenitally glaucomatous eye fell spontaneously after the initial rise following the use of "DFP." In the eye with chronic simple glaucoma an iridectomy ab externo had to be performed to bring the tension back to its former level. These observations must be kept in mind in starting "DFP" therapy with any patient.

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EFFECT OF DIISOPROPYL FLUOROPHOSPHATE ("DFP") ON THE NORMAL EYE

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DURING the past few years many investigators [1] have studied the physiologic and pathologic effects of the fluorophosphates. Of these, the diisopropyl derivative ("DFP") has received most attention. It has been shown to be a powerful inhibitor of cholinesterase [2] and therefore has pronounced parasympathomimetic and nicotinic actions. It is much more potent than physostigmine in these respects. In the eye, "DFP" has been shown to produce prolonged and marked miosis, spasm of the ciliary muscle, false myopia and decrease in intraocular tension.[3] The ocular effects of "DFP" far outlast those produced by other known miotic agents. For example, miosis was found to last two days in the rabbit,[4] ten days to two months in the cat [5] and three to nine days [3a] and fourteen to twenty-seven days [3b] in man. The spasm of the ciliary muscle has been found to last three to seven days in man.[6] Because of the

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1. McCombie, H.; Adrian, E. D.; Kilby, B. A., and Kilby, M.: Personal communication to the authors. Bowden, E.; Horton, R. G.; Sober, H. A.; Hunt, G. M., and Ferguson, R. L.: Personal communication to the authors. Wallen, L.; Horton, R. G., and Sober, H. A.: Personal communication to the authors. Adrian, E. C.; Kilby, B. E., and Kilby, M.: Personal communication to the authors.

2. (*a*) Mackworth, J. F.: Personal communication to the authors. (*b*) Koelle, G., and Gilman, A. Z.: Personal communication to the authors. (*c*) Mazur, A., and Bodansky, O.: Personal communication to the authors.

3. (*a*) Scholz, R., and Wallen, L. J.: Personal communication to the authors. (*b*) Loughlin, R. C.: Personal communication to the authors. (*c*) Cullumbine, H.: Personal communication to the authors.

4. Scholz, R.: Personal communication to the authors.

5. Cattell, McK.: Personal communication to the authors.

6. Scholz and Wallen.[3a] It is believed that the prolonged action of "DFP" is due to an actual destruction of the enzyme cholinesterase rather than to a temporary inhibition. Evidence for this concept is found in the observation that the time for the restoration of the original cholinesterase activity of the plasma is about the same as that for the regeneration of plasma proteins and that the

(Footnote continued on next page)

potentialities of this long-acting, powerful miotic agent in the treatment of glaucoma, further studies of its ocular pharmacologic properties were undertaken.

Our studies were directed mainly toward investigating the mode of action of "DFP," the possibilities of systemic absorption from its local use in the eye and the problem of "DFP"–atropine antagonism. In the course of these studies, we had opportunity to confirm and extend previous observations of other investigators.

RESULTS

A. *Effects on Iris, Ciliary Muscle and Intraocular Tension.*—In all species tested (rabbits, cats, dogs and man) we confirmed the previous reports of intense, prolonged miosis following instillation of "DFP" into the conjunctival sac. Quantitative species variations were found to exist, but the effect of the drug was most marked and prolonged in man, in whom maximal pupillary constriction occurred after instillation of 0.1 per cent "DFP" in water or in peanut oil [7] and some miosis persisted for six to twenty-seven days (table 1).[8] The miosis began within five to ten minutes and was maximal within fifteen to twenty minutes. The pupils constricted slightly more rapidly after instillation of "DFP" in water, though the intensity and duration of the response were approximately equal for the solutions in oil and in water. Lower concentrations of "DFP" have been employed in glaucomatous human eyes. No effect on size of the pupil was noted when concentrations below 0.01 per cent were used, and the lowest concentration which produced maximal pupillary constriction in some of these eyes was 0.05 per cent in oil.[9]

The speed and intensity of the pupillary response to 0.1 per cent "DFP," therefore, are equal to or greater than those reported for 1 per cent physostigmine salicylate and 5 per cent neostigmine bromide in man.[10] The duration of response to "DFP" is much greater than that of any other known miotic agent.

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time for the restoration of the cholinesterase activity of the red blood cells parallels that of the regeneration of the red cells (Koelle and Gilman.[2b] Mazur and Bodansky [2c]).

7. Maximal constriction occurred in rabbits after instillation of 0.1 per cent "DFP" (in oil or water) and in cats and dogs after 1 per cent solution (in water).

8. The duration never exceeded forty-eight hours in rabbits (0.1 per cent concentration in oil or water), two to six days in cats (1 per cent in water) or two to ten days in dogs (1 per cent in water).

9. Leopold, I. H., and Comroe, J. H., Jr.: Use of Diisopropyl Fluorophosphate ("DFP") in Treatment of Glaucoma, Arch. Ophth., this issue, p. 1.

10. Duke-Elder, W. S.: Text Book of Ophthalmology, London, Henry Kimpton, 1932, vol. 1, p. 518. Kull, J.: Ophthalmologica **104**:23, 1942.

TABLE 1.—*Effect of Diisopropyl Fluorophosphate ("DFP") on Size of Pupil in Man* *

Patient	Sex	Age	Color of Eyes	Initial Size of Pupil, Mm.	Oil or Water Solution	Size of Pupil Following Instillation of 0.1 per Cent "DFP," Mm., Days									Comment
						2d	4th	6th	8th	10th	14th	17th	20th	27th	
1. L. F.	M	56	Hazel	O.S. 3	Water	1	2	2	2.5	2	2	2	2	2	Blurred vision and headaches
				O.D. 3	Oil	1	2	2	2.5	2	2	2	2	2	2 days; ciliary injection 10 days
2. R. G.	M	20	Blue	O.S. 4	Water	1	2.5	2.5	3.5	2	5	..	3	..	Blurred vision and ciliary injection
				O.D. 4	Oil	1	2	2	3	2	4	..	2.5	..	2 days; headache 6 days
3. T. H.	M	17	Blue	O.S. 3	Water	1	3	4	4	3	..	..	..	..	Headache, blurred vision and ciliary
				O.D. 3	Oil	1	3	4	4	3	..	..	..	..	injection 2 days
4. R. S.	M	20	Blue	O.S. 3	Water	1	2	2	..	..	..	..	..	..	Blurred vision 6 days
				O.D. 3	Oil	1	2	2	..	..	..	..	..	..	
5. P. S.	F	23	Blue	O.S. 5	Water	1	2.5	3.5	4	..	4	4	4	5	Ciliary injection and pain in eyes
				O.D. 5	Oil	1	2	3	4	..	4	4	4	5	2 days; blurred vision 14 days
6. R. C.	F	44	Blue	O.S. 5	Water	1	1.5	2.5	..	2	3	3	2	3	Pain and ciliary injection 2 days
				O.D. 5	Oil	1	1.5	2.5	..	2	3	3	2	3	

* Three drops of 0.1 per cent "DFP" in oil was instilled at thirty second intervals into the right eye, and 3 drops of 0.1 per cent "DFP" in water, into the left eye. Patient 4 left the hospital at the end of six days, while his pupils were still constricted.

A more precise comparison of the speed and intensity of miosis produced by "DFP" and by neostigmine was made in cats and dogs. As shown in table 2, 1 per cent "DFP" usually produced more prompt and more pronounced miosis in cats than did 5 per cent neostigmine bromide. In all instances "DFP" produced much more prolonged miosis

TABLE 2.—*Comparison of Influence of 5 per Cent Neostigmine Bromide and 1 per Cent "DFP" on Size of Pupil of Cat and Dog*

	Animal	Number	Onset of Miosis, Min.	Minimal Size of Pupil, Min.	Time for Minimal Size, Min.
5 per cent neostigmine bromide	Cat	14	10-40	1.5-8	26-115
	Dog	7	5-10	0.5-1	20-37
1 per cent "DFP"	Cat	6	16-19	1-2	15-40
	Dog	3	8-12	1-3	15-30

than did neostigmine, since pupillary constriction produced by the latter never lasted as long as twenty-four hours.

In the present study we did not measure the effect of the ciliary muscle of normal eyes. However, data are presented in table 3 showing the refractive error before and after the instillation of "DFP" in 5 patients with glaucoma. In each patient "DFP" produced a false myopia which was maximal within one hour and gradually lessened in the

TABLE 4.—*Influence of "DFP" on Intraocular Tension of Normal Human Eyes**

		Tension, Mm. Hg.						
Patient	Eye	Prior to "DFP"	5 Min. After "DFP"	24 Hr. After "DFP"	4 Days After "DFP"	6 Days After "DFP"	8 Days After "DFP"	27 Days After "DFP"
L. F.	O.D.	19	16	13	15	17	18	18
	O.S.	19	17	13	15	16	19	19
R. G.	O.D.	22	20	15	15	15	19	..
	O.S.	20	19	13	15	15	20	..
T. H.	O.D.	23	19	15	19	20	22	..
	O.S.	19	17	11	19	19	20	..
R. S.	O.D.	21	20	11	11	15	..	..
	O.S.	21	20	13	13	15	..	..
P. S.	O.D.	19	16	10	13	13	16	19
	O.S.	18	16	10	13	16	17	19
R. C.	O.D.	20	17	11	13	15	..	19
	O.S.	20	18	11	13	13	..	21

* The subjects and experimental conditions are the same as those presented in table 1.

next forty-eight hours. These data confirm the observations of Scholz and Wallen [3a] that "DFP" is capable of producing ciliary spasm.

Intraocular tension was recorded (Schiøtz tonometer) in 6 normal persons before and after instillation of 0.1 per cent "DFP." The intraocular tension fell in all 12 eyes (table 4). A decrease could be detected within five minutes in 3 patients. The maximal depression occurred within twenty-four hours. It returned slowly to normal, and in eight days

TABLE 3.—*Influence of 0.05 per Cent "DFP" in Peanut Oil on Refractive Errors of Glaucomatous Eyes*

No.	Patient	Eye	Manifest Refractive Error			
			Before "DFP"	1 Hr. After "DFP"	24 Hr. After "DFP"	48 Hr. After "DFP"
8.	R. R.	O.D.	−4.00 ⊃ + 1.00, ax. 90	−8.00 ⊃ + 1.00, ax. 90	−6.00 ⊃ + 1.00, ax. 90	−5.00 ⊃ + 1.00, ax. 90
6.	M. S.	O.D.	+ 25, ax. 90	−5.00 ⊃ + 25, ax. 90	−5.00 ⊃ + 25, ax. 90	−3.50 ⊃ + 25, ax. 90
		O.S.	+ 50, ax. 90	−5.00 ⊃ + 50, ax. 90	−3.00 ⊃ + 50, ax. 90	−1.75 ⊃ + 50, ax. 90
12.	M. M.	O.S.	+1.00 ⊃ + 37, ax. 105	−3.00 ⊃ + 37, ax. 105	−2.50 ⊃ + 37, ax. 105	−2.00 ⊃ + 37, ax. 105
16.	E. M.	O.S.	+ 75 ⊃ + 75, ax. 175	−2.00 ⊃ + 75, ax. 175	−1.75 ⊃ + 75, ax. 175	−1.00 ⊃ + 75, ax. 175
19.	D. G.	O.D.	+1.75 ⊃ + 50, ax. 160	− 75 ⊃ + 50, ax. 160	+1.00 ⊃ + 50, ax. 160	+1.50 ⊃ + 50, ax. 160

recovery was almost complete, though one eye showed a slightly lowered tension on the twenty-seventh day. These data are essentially the same as those reported by Scholz and Wallen,[3a] although these authors described a transient rise in 1 of 12 men examined after instillation of "DFP." The effects of "DFP" on glaucomatous eyes are recorded in detail elsewhere.[9] However, it is worthy of mention that intraocular tension was lowered in several eyes with previous iridectomy in which no noticeable pupillary constriction occurred. In the other eyes, the decrease in tension was accompanied with pupillary constriction.

As would be expected from these ocular effects, many patients complained of blurred distant vision, difficulty in adjusting from near to distant objects and aching of the brow and eye after instillation of "DFP." The ocular pain often became more severe with close work. These symptoms are due largely to ciliary spasm and have been noted previously.[3a,c] Further details are included in a report of observations on 52 patients with glaucoma treated with "DFP." [9]

B. *Site of Action of "DFP" on Iris.*—The site of action of "DFP" on the iris was investigated in order to determine whether the drug acts entirely by inactivation of cholinesterase or partly by direct action of "DFP" on the muscle of the iris. It has been shown by Anderson [11] that physostigmine constricts the pupil in normal cats but fails to do so after the ciliary ganglion has been removed and time allowed for degeneration of the postganglionic fibers. While these results have never been disputed so far as the iris muscle is concerned, some investigators [12] have produced evidence that physostigmine has a direct action on striated skeletal muscle. Similar experiments on the eye have not been recorded for "DFP."

Methods: Cats were selected for these experiments, since complete ciliary ganglionectomy is extremely difficult in the dog and the rabbit. (We operated on 10 dogs, but in no instance were we able to obtain reactions consistent with a complete ciliary ganglionectomy that persisted over a period long enough for evaluation of all the drugs concerned.) Cats were anesthetized with sodium pentobarbital given intravenously or intraperitoneally. The hair was removed from the region of the left eye; the lids were sutured together, and an incision in the skin was made below and lateral to the orbit. A portion of the zygoma and the lateral wall of the orbit was removed. The conjunctiva and Tenon's capsule were opened, and the external rectus muscle was identified. This muscle was elevated by means of a retractor, and the ciliary ganglion was exposed. If difficulty was encountered, the nerve from the inferior oblique muscle was traced back to its branch which leads to the ciliary ganglion. The ganglion was grasped with a fine hemostat; all branches were severed, and the ganglion was removed. The incision was then sutured and the wound flushed with solution of penicillin. No wound infections occurred. Since the operation abolished

11. Anderson, H. K.: J. Physiol. **33**:156 and 414, 1905.

12. Brown, G. L., and Harvey, A. M.: J. Physiol. **99**:379, 1941.

corneal sensitivity and secretions at least temporarily, the chief postoperative complication was desiccation and ulceration of the cornea. A number of cats had to be discarded for this reason.

In some cats the left superior cervical ganglion was also removed. This ganglion was extirpated completely after it was distinguished from the vagus ganglion at the level of the carotid sinus.

The criteria of a complete ciliary ganglionectomy were (*a*) dilation of the pupil on the side of operation, (*b*) failure of the iris to react to strong light, (*c*) sensitivity to 0.5 per cent pilocarpine nitrate and 20 per cent mecholyl bromide on the side of operation and (*d*) failure of 2 per cent physostigmine salicylate to constrict this pupil.

The solutions were freshly prepared from redistilled "DFP."[13] Each sample had been sealed in a glass ampule and kept in the ice box until just before dilution. Although lower concentrations of "DFP" are miotic, a 1 per cent solution in water was employed in these experiments in order to attain a high concentration of the drug within the eye. Two drops (0.1 cc.) was instilled into the lower conjunctival sac of the right eye and 3 drops (0.15 cc.) in the left eye; in this manner we were sure that the amount of "DFP" received by the denervated iris was at least equal to and probably greater than the amount received by the normal iris. Pupillary sizes were measured with a millimeter rule in the dimmest light compatible with accurate reading (unless otherwise stated); this light was kept constant throughout the experiments. At no time were the cats exposed to bright sunlight. The 5 cats used in this experiment had been operated on eighteen to twenty-one days before instillation of "DFP."

Results: In 4 cats, 1 per cent "DFP" in water had no effect whatever on pupillary size on the denervated side, the pupil remaining widely dilated throughout (table 5). In cat 6 the pupil constricted from a diameter of 12 mm. to one of 7 mm. However, it is unlikely that this represents a direct action of the drug on the denervated muscle of the iris, since instillation of 1 per cent atropine sulfate promptly dilated the pupil fully; it more likely indicates an incomplete ganglionectomy.

The failure of the pupil on the ganglionectomized side to react is not due to decreased permeability of the cornea following the operation. It can be inferred from table 5 that the effect of "DFP" lasted as many days on the left side as on the right, for the following reason: While the pupil on the right (intact) side returned to its control size within fifty-two hours in 4 of the 5 cats, it remained abnormally sensitive to light for nine to thirteen days. This sensitivity to light is due, we believe, to a continued lack of cholinesterase in the iris muscle. Bright light in the eye reflexly increases the parasympathetic impulses to the normal iris and so increases the formation of acetylcholine at the nerve endings. Because of the increased acetylcholine and the decreased cholinesterase, the muscle contracts more strongly to light and relaxes more slowly in dim light. Since ciliary ganglionectomy interrupts the pathway of the

13. Obtained from the Medical Division, Chemical Warfare Service, Edgewood Arsenal, Md.

light reflex, we could not use the same technic on the left (denervated) side, in order to determine the length of the anticholinesterase effect of "DFP." Therefore, local instillation of 1 per cent acetylcholine bromide was employed. In each instance, after administration of "DFP" the left pupil constricted definitely after instillation of this concentration of acetylcholine, whereas before administration of "DFP," 10 per cent acetylcholine bromide was usually without effect.[14] This reaction to acet-

TABLE 5.—*Effect of 1 per Cent "DFP" in Water on Size of Pupil (Mm.) in Normal (O.D.) Eyes and in Eyes After Ciliary Ganglionectomy (O.S.) with Cervical Sympathetic Ganglions Intact**

	Cat 3		Cat 4		Cat 6		Cat 7		Cat 8	
Time	O.D.*	O.S.	O.D.	O.S.	O.D.	O.S.	O.D.	O.S.	O.D.	O.S.
Control.....	11	12	10	12	10	12	9.5	12	11	12
1% "DFP" in water—2 drops, O.D.; 3 drops, O.S.										
15 min.....	9.0	12	7.0	12	0.5	12	5.0	12	0.9	12
25 min.....	1.0	12	2.0	12	0.5	8	0.5	12	2.0	12
40 min.....	0.5	12	0.5	12	0.5	7	0.5	12	0.5	12
55 min.....	0.5	12	0.5	12	0.5	7	0.5	12	0.5	12
75 min.....	0.5	12	0.5	12	0.5	7	0.5	12	0.5	12
4 hr.....	1.0	12	1.0	12	1.0	7	0.5	12	0.5	12
						1% atropine				
5 hr.....	1.5	12	2.0	12	4.0	12	0.5	12	1.0	12
22 hr.....	9.0	12	5.0	12	7.0	12	3.0	12	9.0	12
47 hr.....	11.0	12	10.0	12	9.0	12	7.0	12	10.0	12
52 hr.....	11.0	12	10.5	12	9.0	12	4.5	12	11.0	12
53 hr.....	11.0	12	11.0	12	10.0	12	8.0	12	11.0	12
	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.
3 days.....	11.0	12	10.0	12	10.0	12	8.0	12	11.0	12
	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.
6 days.....	11.0	12	10.0	12	10.0	12	8.0	12	11.0	12
	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.
9 days.....	11.0	12	10.0	12	10.0	12	9.0	12	11.0	12
	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.	L.S.	A.Ch.
13 days.....	11.0	12	10.0	12	10.0	12	9.0	12	11.0	12
			L.S.		L.S.		L.S.		L.S.	A.Ch.
19 days.....	11.0	12	10.0	12	10.0	12	9.0	12	11.0	12

* L.S. indicates that the eye was light sensitive, and A.Ch. that it was acetylcholine sensitive. Numbers above L.S. and A.Ch. refer to size of pupil before procedure.

ylcholine lasted nine to thirteen days. In other words, though different criteria were employed, it appears that the effect of "DFP" on the intact and on the denervated eye was equal in duration, and by inference the same amount of "DFP" reached each iris and exerted the same anticholinesterase action locally. It is concluded, therefore, that "DFP" in the concentrations used has no effect on the iris muscle itself.

"DFP" (1 per cent in water) was instilled into the eyes of a sixth cat, in which both the left ciliary and the left superior cervical ganglion were removed. Though the right eye responded to the drug with pro-

14. Even ganglionectomized eyes did not respond with miosis to 10 per cent acetylcholine bromide if "DFP" had not been instilled. This indicates that the tissues of the cat eye must be able to inactivate acetylcholine even in high concentration.

nounced miosis, the pupil of the left eye remained unchanged in size. It had been thought that a weak constrictor action of "DFP" exerted directly on the iris muscle might be obscured by the existence and opposition of tonic dilator sympathetic impulses. These results indicate that "DFP," in the concentration used, has no effect whatever on the iris during the period of complete denervation.

C. *Effect of "DFP" on Homatropinized and Atropinized eyes.*—The high potency of "DFP" made it appear likely that it could overcome the action of homatropine, or even that of atropine, on the eye. Consequently, we evaluated the "DFP"–homatropine antagonism in 5 young adults (18 to 23 years) and the "DFP"–atropine antagonism in 6 children (8 to 12 years) and 5 adults (17 to 54 years). In the first group (table 6) 3 drops of 4 per cent homatropine hydrobromide was instilled at fifteen minute intervals; one hour and fifteen minutes after the last drop, 2 drops of "DFP" in peanut oil was instilled into each eye. The eyes of the 6 children in the second group were atropinized in the following manner: One drop of 0.5 per cent atropine sulfate was instilled into each conjunctival sac. Another drop was instilled at intervals of twelve, sixteen, twenty-two and thirty-six hours. One hour and forty-five minutes after the last (fifth) drop of atropine sulfate, 2 drops of 0.05 per cent "DFP" in peanut oil was instilled into both eyes of 4 children, and 2 drops of a 0.1 per cent concentration of "DFP" in oil into both eyes of the other 2 children. The eyes of the 5 adults in the third group were atropinized by placing 2 drops of 1 per cent atropine sulfate at intervals of one minute into both eyes. One hour later, 0.1 per cent (2 patients) or 0.2 per cent (3 patients) of "DFP" in oil was instilled. In all these patients the pupils were measured at regular intervals and the near points determined with a Duane line; in the last 5 patients visual acuities also were measured, employing a Snellen test chart.

From the data recorded in table 6, it is evident that in every eye previously homatropinized or atropinized "DFP" constricted the pupil and augmented the accommodation. The intensity of the effect of the drug varied. In 0.05 per cent concentration it completely overcame the influence of 4 per cent homatropine hydrobromide on the ciliary body and the musculature of the iris. In the eyes of the children, 0.05 per cent "DFP" always augmented the accommodation and constricted the pupil, but the effect of the drug lasted only twenty-four to forty-eight hours. The 0.1 per cent concentration had a greater effect. In adults, 0.1 and 0.2 per cent, "DFP" overcame the effects of atropine and lasted six to nine days.

It is interesting to note that only 0.2 per cent solution of "DFP" was required to overcome the action of 1 per cent atropine sulfate on the muscles of the iris and ciliary body. The ability of "DFP" to antagonize

TABLE 6.—*Influence of "DFP" on Homatropinized or Atropinized Human Pupils*

Patient *	Age, Yr.	Eye	Near Points, Cm.									Pupillary Size, Cm.								
					Time After "DFP"									Time After "DFP"						
						Days									Days					
			Control	After Cycloplegia	1 Hr.	1	2	3	4	5	6	Control	After Cycloplegia	1 Hr.	1	2	3	4	5	6
A. Homatropinized Adult Eyes																				
1. H. H.	23	O.D.	11	40	7	7	7	..	9	..	..	4.5	9	2.5	2.5	..	..	3	..	..
		O.S.	11	40	7	7	7	..	9	..	..	4.5	9	2	2.5	..	..	3	..	..
2. A. G.	23	O.D.	10	45	7	7	8	..	..	..	..	4	9	1	2	..	..	..	..	..
		O.S.	10	48	7	7	7.5	..	..	..	..	4	9	1	2	..	..	..	..	..
3. H. A.	18	O.D.	9	50+	8	8	8	..	..	..	..	3.5	8	1	1.5	..	..	..	2	..
		O.S.	9	50+	8.5	8	8	..	..	..	..	3.5	8	1	2	..	..	..	2	..
4. R. D.	20	O.D.	10	45	7.5	..	7.5	..	..	..	..	5	8	1	2	..	..	..	..	..
		O.S.	10	49	7	..	7.5	..	..	..	..	5	8	1	1	..	..	..	..	..
5. M. H.	19	O.D.	9	50+	7	..	..	7	..	..	8	5	7	1	1	..	..	..	..	3
		O.S.	9	50+	7	..	..	7	..	..	8	5	7	1.5	1.5	..	..	..	..	3
B. Atropinized Children's Eyes																				
6. B. B.	10	O.D.	6	50+	10	10	12	..	..	..	..	3	9	4	8	..	..	..	..	..
		O.S.	6	50+	20	20	23	..	..	..	..	3	9	7	8	..	..	..	..	..
7. C. J.	12	O.D.	6.5	50+	9	12	..	..	..	..	..	3	9	3	7	..	..	..	..	..
		O.S.	7	50+	25	25	..	..	..	..	..	3	9	8	9	..	..	..	..	..
8. J. C.	9	O.D.	5	50+	20	20	..	..	..	..	..	5	9	7	9	..	..	..	..	..
		O.S.	6	50+	12	12	..	..	..	..	..	5	9	5	7	..	..	..	..	..
9. R. S.	10	O.D.	5	50+	10	10	..	..	..	..	..	4	9	4	7	..	..	..	..	..
		O.S.	5	50+	20	20	..	..	..	..	..	4	9	7	8	..	..	..	..	..
10. B. R.	10	O.D.	5	50+	6	6	..	..	..	..	..	3	9	2	6	..	..	..	..	..
		O.S.	5	50+	6	6	..	..	..	..	..	3	9	2	7	..	..	..	..	..
11. G. R.	8	O.D.	5	50	7	7	..	..	..	..	..	3	9	1	5	..	..	..	..	..
		O.S.	5	50	6	7	..	..	..	..	..	3	9	1	5	..	..	..	..	..

C. Atropinized Adult Eyes

Patient †	Age, Yr.	Eye	Control	After Cycloplegia	Time After "DFP"							
					1 Hr.	3 Hr.	Days 1	2	3	4	5	6	9
			Near Points, Cm.										
1. C. B.	17	O.D.	9	40	40	40	40	33	33	..	..	..	..
		O.S.	8.5	44	11	8	8	7	7	..	..	..	..

2. W. P.	30	O.D.	10	50+	50	15	10	10	10	..	10	..	10
		O.S.	10	50+	50	25	10	10	10	..	10	..	10
3. M. W.	18	O.D.	9	40	40	40	40	38	30	..	30	..	12
		O.S.	9	40	30	9	9	9	9	..	9	..	9
4. P. A.	25	O.D.	12	48	48	48	40	..	40	30	..	..	12
		O.S.	12	45	11	11	11	..	12	11	..	..	12
5. H. H.	54	O.D.	27	50+	50+	50+	50+	50+	50	..	50	50	27
		O.S.	26	50+	45	25	25	25	25	..	25	25	25
						Size of Pupil, Cm.							
1. C. B.	17	O.D.	5	9	9	9	9	8	8.5	..	..	..	..
		O.S.	5	9	4	3	3	2	3.5	..	..	..	..
2. W. P.	30	O.D.	7	9	8	6	2	2	3	..	6	..	7
		O.S.	7	9	9	8	2	2	3	..	6	..	7
3. M. W.	18	O.D.	5	9	9	9	9	8.5	8	..	8	..	5
		O.S.	5	9	7	3	3	3	3	..	3	..	5
4. P. A.	25	O.D.	4	9	9	9	9	..	9	8	..	..	4
		O.S.	4	9	1.5	1.5	1.5	..	2.5	3	..	..	4
5. H. H.	54	O.D.	5	8	8	8	7	7	6	..	..	6	5
		O.S.	5	8	6	4	5	3	3	3.5	..	3.5	4
						Visual Acuity							
1. C. B.	17	O.D.	6/6	6/20	6/20	6/20	6/9	....	6/6	....	....	....	....
		O.S.	6/6	6/15	6/6-2	6/60	6/6 (−6S)‡	....	6/6 (−6S)	....	....	....	....
2. W. P.	30	O.D.	6/20	6/30	....	....	....	....	6/20	....	....	....	....
		O.S.	6/15	6/20	....	....	....	....	6/6 (−5S)	....	....	....	....
3. M. W.	18	O.D.	6/6+	6/20	6/20	6/20	6/20	6/20	6/15	....	....	....	6/9+2
		O.S.	6/6+	6/20	6/6	6/6	6/6 (−2S)	6/6 (−3S)	....	....	....	....	6/6+
4. P. A.	25	O.D.	6/12	6/60	6/60	6/60	6/60	....	6/12	....	....	....	6/12+
		O.S.	6/6	6/22	6/6	6/6	6/6	....	6/6 (−2S)	....	....	....	6/6
5. H. H.	54	O.D.	6/9	6/30	6/30	6/30	6/20	....	6/9	....	....	....	6/6+6
		O.S.	6/6	6/20	6/15	6/6-1	6/6-1 (−1S)	....	6/6 (−1S)	....	....	....	6/6

* Patients 1 to 5, inclusive, had 3 drops of 4 per cent homatropine hydrobromide at fifteen minute intervals in both eyes; seventy-five minutes later 1 drop of 0.05 per cent "DFP" was instilled in both eyes. Patients 6 to 9, inclusive, had 5 drops of 0.5 per cent atropine sulfate in both eyes over a period of thirty-six hours; 2 drops of 0.05 per cent "DFP" was instilled seventy-five minutes after the last drop of atropine. Patients 10 and 11 had 5 drops of 0.5 per cent atropine sulfate (like patients 6 to 9), followed by 2 drops of 0.1 per cent "DFP" seventy-five minutes after the last drop of atropine.

† Patients 1 and 2 had 2 drops of 1 per cent atropine sulfate in both eyes, followed one hour later by 2 drops of 0.1 per cent "DFP" in oil in each left eye and also 1 drop of 0.1 per cent "DFP" in the right eye of patient 2. Patients 3, 4 and 5 had 2 drops of 1 per cent atropine sulfate in both eyes, followed one hour later by 2 drops of 0.2 per cent "DFP" in oil in each left eye.

‡ Indicates minus diopters sphere required for best visual acuity.

atropine should be of value in ophthalmology. Other drugs used at present for the purpose are not satisfactory. Histamine in strong concentration is a powerful miotic but, unfortunately, causes considerable chemosis and inflammation of the conjunctivas and lids and is very painful. In order for physostigmine to constrict an atropinized pupil and maintain such antagonistic miosis, it must be used in concentration equal to or greater than the concentration of atropine and must be used repeatedly. Even then, in many instances, it may fail to produce an antagonistic effect on the pupil. Pilocarpine and carbaminoylcholine are not so powerful as physostigmine. On the other hand, the present data show that "DFP" will constrict the atropinized pupil in one or two applications, in weaker concentrations than that of the atropine used, and that its effect will persist.

Normal eyes usually show circumcorneal injection after instillation of a drop of "DFP" in oil in concentrations as low as 0.5 per cent. This corneal injection, we believe, is due to the inability of ocular tissues to destroy acetylcholine. After inactivation of cholinesterase by "DFP," the acetylcholine, normally liberated by parasympathetic impulses, persists and spreads to neighboring vessels. None of the atropinized eyes showed this after instillation of "DFP," probably because atropine also antagonizes the effect of acetylcholine on vessels.

D. *Effect of "DFP" on Blood–Aqueous Humor Barrier in the Eye.*—The rate of appearance in the aqueous humor of intravenously administered fluorescein or inulin has been employed as a measure of the rate of diffusion of substance through the capillary membrane.[15]

After the intravenous injection of fluorescein, a greenish discoloration normally appears in the pupillary region of the iris in two to four minutes. After ten to twelve minutes a faint cloud of green fluorescence gradually fills the pupillary area.[15c] In our experiments, we instilled 2 drops of 0.1 per cent "DFP" in oil in the right eye of 12 rabbits; the left eyes were used as controls. Twenty minutes later 0.75 cc. of 5.5 per cent solution of sodium fluorescein per pound of body weight was injected intravenously in each rabbit. The fluorescence was always detected first and much more intensely in the eyes treated with "DFP" and persisted longer in these eyes. The increased permeability to fluorescein lasted less than twenty-four hours, even though the treated eyes were still miotic.

In 6 other rabbits 1 per cent physostigmine salicylate was placed in the left conjunctival sac and 0.1 per cent "DFP" in the right sac.

15 (*a*) Linksz, Q.: Arch. f. Augenh. **104**:264, 1931. (*b*) Gifford, H.: Use of Fluorescein Intravenously as Aid to Ophthalmic Diagnosis and Treatment, Arch. Ophth. **24**:122 (July) 1940. (*c*) Swan, K., and Hart, W.: Am J. Ophth. **23**:1311, 1940.

There were no significant differences in the rate of appearance, intensity of fluorescence or persistence of fluorescence in the two series of eyes.

Five cubic centimeters of a 10 per cent solution of inulin was injected intravenously in 11 rabbits (table 7) fifteen minutes before to twenty-five minutes after instillation of "DFP" into one conjunctival sac. Aqueous humor (from both eyes) and samples of blood were withdrawn fifteen to fifty-eight minutes after instillation of "DFP" and these were analyzed for inulin by the method of Roe.[16] As shown in table 8, there are no significant differences between the two eyes in regard to diffusion of inulin from blood to aqueous humor.

TABLE 7.—*Amounts of Inulin in Blood and Aqueous Humor Following Its Intravenous Injection*

Rabbit Number	Time of Inulin Injection After "DFP" Instillation, Min.	Time of Withdrawal of Blood and Aqueous, Min.	Inulin Recovered, Mg. per Cc.		
			Aqueous		
			O.S. 2% "DFP"	O.D. Control	Blood
1	2	15	0.02	0.22	....
2	3	30	0.05	0.05	0.21
3	3	30	0.12	0.34	0.29
4	15	30	0.00	....	0.15
5	15	30	0.01	0.01	0.19
6	15	30	0.1	0.1	0.42
7	15	30	0.1	0.12	0.42
9	8	50	0.14	0.14	0.46
10	25	55	0.07	0.09	0.32
11	24	58	0.07	0.1	0.22
12	—15	43	0.68	0.79	0.49

These results indicate an increased permeability of the capillaries for fluorescein (a substance of low molecular weight) but not to inulin (a substance of high molecular weight). It is probable that this capillary change is due to arteriolar vasodilation (with consequent increase in capillary pressure) rather than to increased permeability in general, such as might occur after the use of histamine.

E. *Systemic Absorption of "DFP" from the Eye.*—It became evident from observations on cats and dogs that systemic effects may follow the instillation of "DFP" into the conjunctival sac. In 1 of 11 cats, "DFP" (2 drops of a 1 per cent aqueous solution instilled in each eye) produced systemic effects, such as salivation and muscle tremors. While such an effect was much less frequent after 1 per cent solution of "DFP" than after a 5 per cent solution of neostigmine bromide,[17] we felt that the question of systemic absorption should be investigated carefully in man. In several thousand instillations of "DFP" in man there has been no sub-

16. Roe, J. H.: J. Biol. Chem. **107**:15, 1934.

17. In 6 of 11 cats, instillation of 2 drops of 5 per cent neostigmine bromide in water into each eye led to marked and often alarming symptoms of salivation, frothing, dyspnea, diarrhea, vomiting and muscular tremors.

jective or objective evidence of nicotinic action or parasympathomimetic hyperactivity. Nevertheless, determinations of plasma and red cell cholinesterase were performed on 11 patients before and one to two hours after instillation of "DFP" into the conjunctival sac. No significant fall in red cell cholinesterase occurred in any patient after this. Plasma cholinesterase decreased more than 10 per cent in 4 of the 11 patients, the maximal decrease being 29 per cent (table 8). The decrease in plasma cholinesterase in these 4 patients was greater than the fluctuations which occurred normally in the 5 control subjects. It has been shown [2b,c] that plasma cholinesterase is extremely sensitive to "DFP" in man and that red cell cholinesterase is much more resistant. In man plasma cholinesterase may be reduced to 2 to 10 per cent without any appreciable reduction in red cell cholinesterase. Despite a very low plasma cholin-

TABLE 8.—*Plasma and Red Cell Cholinesterase Levels in Eleven Patients Before and After Instillation of 2 Drops of 0.2 per Cent "DFP" into Each Eye and in Five Control Subjects Who Received No Drug*

Initials	Time	Plasma Cholinesterase *	Per Cent Change Plasma Cholinesterase	Red Cell Cholinesterase †
J. C.	Before	17.0	—16	10.2
	1½ hr. after	14.4		11.2
D. G.	Before	10.8	—29	13.0
	1½ hr. after	7.7		12.9
	5 hr. after	8.8		12.9
H. M.	Before	18.4	—23	10.9
	1½ hr. after	14.2		11.4
H. T.	Before	18.1	— 3	15.8
	1½ hr. after	17.6		15.0
B. H.	Before	16.6	— 5	10.0
	1 hr. after	15.7		10.3
R. P.	Before	13.2	— 4	15.7
	1½ hr. after	12.8		15.8
A. R.	Before	17.6	—10	8.6
	2 hr. after	15.9		8.6
E. T.	Before (last drop 11 days ago)	9.0	—10	10.7
	2 hr. after 4 instillations in 8 hr.	8.1		12.3
E. E. B.	Before	18.9	— 23	11.9
	2 hr. after	14.5		11.7
R. B.	Before	13.4	—10	12.4
	2 hr. after	11.9		12.6
W. D.	Before	17.5	+ 7	10.1
	2 hr. after	18.3		11.0
G. N.‡	0 hr	19.7	— 7	11.5
	4 hr	18.3		10.6
A. T.‡	0 hr	6.4	— 8	9.8
	4 hr	5.9		9.2
N. S.‡	0 hr	11.7	— 9	9.9
	4 hr	10.6		10.2
B. W.‡	0 hr	17.1	+ 5	12.9
	4 hr	17.9		12.7
F. G.‡	0 hr	12.9	—13	10.8
	4 hr	11.2		10.7

* Values are expressed in micromols of carbon dioxide per thirty minutes (1:5 dilution).
† Micromols of carbon dioxide per thirty minutes (1:10 dilution).
‡ The last 5 subjects received no drug but are included as controls on the relative constancy of determinations of the cholinesterase.

esterase, symptoms do not appear in man (after a single dose of "DFP") until the red cell cholinesterase is reduced to 70 to 80 per cent. It is evident, therefore, that minimal or insignificant absorption occurred from ocular instillation in these patients. This does not mean, however, that significant absorption will not follow the frequent, indiscriminate local use of "DFP."

F. *Selection of a Vehicle for "DFP."*—Previous studies have shown that "DFP" is unstable in water but relatively stable in peanut oil. Since the existence of a stable preparation is of great importance for clinical use, we investigated more carefully the differences between oily and aqueous solutions. The period over which "DFP" in oil remains potent was measured by preparing a 0.1 per cent solution of "DFP" in peanut oil and instilling 2 drops of this into a rabbit eye each day for a week and thereafter once a week. The solution was kept in closed dropper bottles at room temperature. It has maintained its ability to constrict the pupil maximally for more than three months. A 0.1 per cent solution of "DFP"in water, prepared at the same time and tested in similar manner on the other eye of the same rabbit, began to lose its potency on the fifth day and was entirely without effect on the seventh day.

To determine whether the oily vehicle altered the rate, intensity and duration of the effect of "DFP" on the eye, a comparison of the effects produced by oily and by aqueous solutions was made in rabbit and in human eyes. Two drops of 0.01, 0.05 or 0.1 per cent "DFP" in peanut oil was instilled into one eye, and a similar dose of aqueous solutions (freshly prepared) into the other eye, of a series of 20 rabbits. There was no significant difference in the rate, intensity or duration of pupillary constriction in these eyes.

Similar experiments were carried out on 6 normal human subjects, using solutions of 0.1 per cent "DFP" in water and in oil (table 1). These results, again, failed to demonstrate a significant difference between the effects produced by the oily and those produced by the aqueous solutions of "DFP."

Some difference has been found in experiments on cats: A 0.2 per cent solution of "DFP" in water produced pupillary constriction which began sooner, lasted longer and was more intense than that produced by 0.2 per cent "DFP" in oil.

SUMMARY

1. Diisopropyl fluorophosphate "DFP" locally instilled in the eye in low concentrations will produce prolonged miosis, ciliary spasm, false myopia and decrease in intraocular tension. Quantative species variations were found to exist, but the effects were most marked and prolonged in man.

2. A 1 per cent solution of "DFP" produced more prompt, pronounced and prolonged miosis than a 5 per cent solution of neostigmine bromide.

3. "DFP" in the concentrations used has no direct effect on the iris muscle itself, since it failed to constrict the totally denervated cat iris. Its effects, therefore, are due entirely to inactivation of cholinesterase.

4. A 0.1 per cent solution of "DFP" was able to overcome the cycloplegic effect in human eyes of 4 per cent homatropine hydrobromide, and a 0.2 per cent solution of "DFP," that of 1 per cent atropine sulfate.

5. "DFP" was shown to increase the capillary permeability for fluorescein but not for inulin.

6. A slight decrease in the plasma cholinesterase was noted after ocular instillation of "DFP," indicating that minimal systemic absorption occurred.

7. No significant difference could be demonstrated between oil and water as a vehicle for "DFP" for ophthalmic use except that "DFP" is decidedly more stable in peanut oil than in water.

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VISUAL DISTURBANCES ASSOCIATED WITH HEAD INJURIES

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THE large number of head injuries observed in battle casualties provides the best material for study of the representation of various areas of the retina in the cerebral cortex. Few contributions have been made from injuries sustained outside of war periods.

Experimental determination of field defects by induced injuries is not feasible, for obvious reasons. One, therefore, must depend on lesions of the brain in human subjects studied at operation or at necropsy. From patients so studied one can draw certain conclusions concerning those who do not come to operation or to necropsy.

The two most significant papers on the subject are those by Holmes and Lister,[1] in 1916, and by Holmes,[2] in 1918, in which they reported their studies of disturbances of vision by cerebral lesions observed in British casualties in World War I.

Henschen,[3] in 1900, had pioneered with pathologic studies showing that the visual cortex lay in the occipital region, and he localized several areas as representing various portions of the retina.

In 1909 Inouye[4] reported the effects of injuries to the occipital lobe incurred in the Russo-Japanese War and pointed out that the macular center was at or near the occipital pole.

Marie and Chatelin,[5] in 1914, reported a similar series of cases. Riddoch[6] later published case reports which confirmed previous observations.

Read before the Ophthalmic Club of Philadelphia, March 6, 1945.

1. Holmes, G. H., and Lister, W. T.: Disturbance of Vision from Cerebral Lesions, Brain **39**:34, 1916.

2. Holmes, G. H.: Disturbances of Vision by Cerebral Lesions, Brit. J. Ophth. **2**:253, 1918.

3. Henschen: Sur le centre cortical de la vision, Cong. internat. de méd., sect. d'opht., Paris, 1900, pt. 9, p. 232.

4. Inouye: Die Sehstörungen bei Schussverletzungen der kortikalen Sehsphäre, nach Beobachtung von Verwundeten der letzen japanischen Kriege, Leipzig, W. Engelmann, 1909.

5. Marie, P., and Chatelin, C.: Les troubles visuels dus aux lésions des voies optiques intracérébrales et de la sphere visuelle corticale dans les blessures du crâne par coup de feu, Rev. neurol. **27**:882, 1914-1915.

(Footnotes continued on next page)

Moreau,[7] in 1918, discussed central field defects in a paper on occipital lesions. He divided the retina into three zones: those of fixation, distinction and perception, and stated the belief that cortical representation was similarly divided.

Morax[8] differentiated the fixation area and the macular area and stated that he had not found the fixation area affected in cases of unilateral lesions but did so when both occipital lobes were injured.

The lesions to be studied involved the chiasm, the optic radiations and the occipital cortex. The anatomy and physiology of the chiasmal fibers require no discussion. The geniculocalcarine pathway lies in the internal capsule behind the sensory fibers and internal to the auditory fibers. Fibers from the upper retinal quadrants lie dorsally, while fibers from the lower retinal quadrants lie ventrally. The macular fibers lie between these two bundles. To the best of present knowledge, the visual cortex occupies the medial surface of each occipital lobe from the occipital pole to the anterior end of the calcarine fissure. Posteriorly, the visual area extends a little onto the lateral surface of each occipital lobe. This area is thought to include representation of the fixation area. Opinion is divided as to whether there is bilateral cortical representation of the macular areas. The consensus is that each cortical macular center represents half of each macula; that is, the left cortex represents the right half of each fixation area and vice versa. This must be so as there is division of the fixation area of the field of each eye when the entire occipital cortex on one side is damaged. The so-called sparing of the macula is the rule with vascular disease but is less frequent with traumatic lesions. Sparing of the entire fixation area is less frequently found when the central field is closely studied. One then finds division of the fixation area rather frequent. There are three reasons for sparing of the fixation area: (1) this area of the cortex may escape from injury; (2) there are two blood supplies to the occipital cortex, the calcarine artery and the middle cerebral artery, and (3) patients may learn to use eccentric vision, particularly when the fixation area is divided. In cases of vascular accident only one of the two arteries is usually occluded, and hence sparing of fixation is the rule. In cases

6. Riddoch, G.: On the Relative Perceptions of Movement and a Stationary Object in Certain Visual Disturbances Due to Occipital Injuries, Proc. Roy. Soc. Med. (Sect. Neurol.) **10**:13, 1916-1917.

7. Moreau, F.: Sur les troubles de la vision maculaire produit par les lésions traumatiques de la région occipitales, Ann. d'ocul. **155**:357, 1918.

8. Morax, V.: Discussion des hypothèses faites sur les connexions corticales des faisceaux maculaires, Ann. d'ocul. **156**:25, 1918.

of traumatic lesions both arteries may be damaged or the entire cortex destroyed.

It is interesting to note that the cortical representation of the macula is rather large as compared with the area representing the more extensive peripheral portions of the retina. This is analogous to the large motor and sensory areas in the parietal cortex representing the finger and thumb as compared with the areas representing the trunk and the extremities.

In the area striata the periphery of the retina is represented near the anterior end of the calcarine fissure. Lesions in this area usually include damage to the optic radiations, and few authentic cases have been recorded in which isolated injury to this area was present. One case of Holmes and Lister's, 2 of Scarlett and Ingham's [9] and cases 8 and 9 of the present series may represent such injuries, but damage to the radiations cannot be excluded in any of these cases. The upper portion of each retina is represented on the area above the calcarine fissure, while the lower portion of the retina is represented in the area below the calcarine fissure. When the area below the calcarine fissure is injured, one should see a defect in the upper fields of vision. The explanation for the infrequency of such defects is that wounds in this area often result in death because of injury to the cerebellum and large blood vessels.

Traquair [10] stated that traumatic lesions of the optic nerve and occipital lobe are frequent, whereas trauma to the chiasm is rare, and that lesions in the geniculate pathway are more often vascular than traumatic in origin.

Riddoch [11] and Holmes [12] have secured interesting data regarding the dissociation of visual perceptions due to injury to the occipital lobes. They pointed out that patients may see movement in the blind field and discussed the prognostic value of this phenomenon. They expressed the opinion that such lesions probably were located in the region of the supramarginal and angular gyri in the parietal lobe. While there is a suggestion in the histories of some of the cases here reported that such dissociations were present, this point has not been studied.

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9. Scarlett, H. U., and Ingham, S. D.: Visual Defects Caused by Occipital Lobe Lesions: Report of Thirteen Cases, Arch. Neurol. & Psychiat. **8**:225 (Sept.) 1922.

10. Traquair, H. M.: An Introduction to Clinical Perimetry, ed. 4, London, Henry Kimpton, 1942.

11. Riddoch, G.: Dissociations of Visual Perceptions Due to Occipital Injuries with Especial Reference to Appreciation of Movement, Brain **40**:15, 1917; Visual Disorientation in Homonymous Half-Fields, ibid. **58**:376, 1935.

12. Holmes, G. H.: Disturbance of Visual Orientation, Brit. M. J. **2**:449 and 506, 1918.

The following 12 cases represent a variety of defects in the visual field which can be traced to a known type and site of injury, with supporting evidence obtained from reports of the neurosurgeon and the roentgenologist.

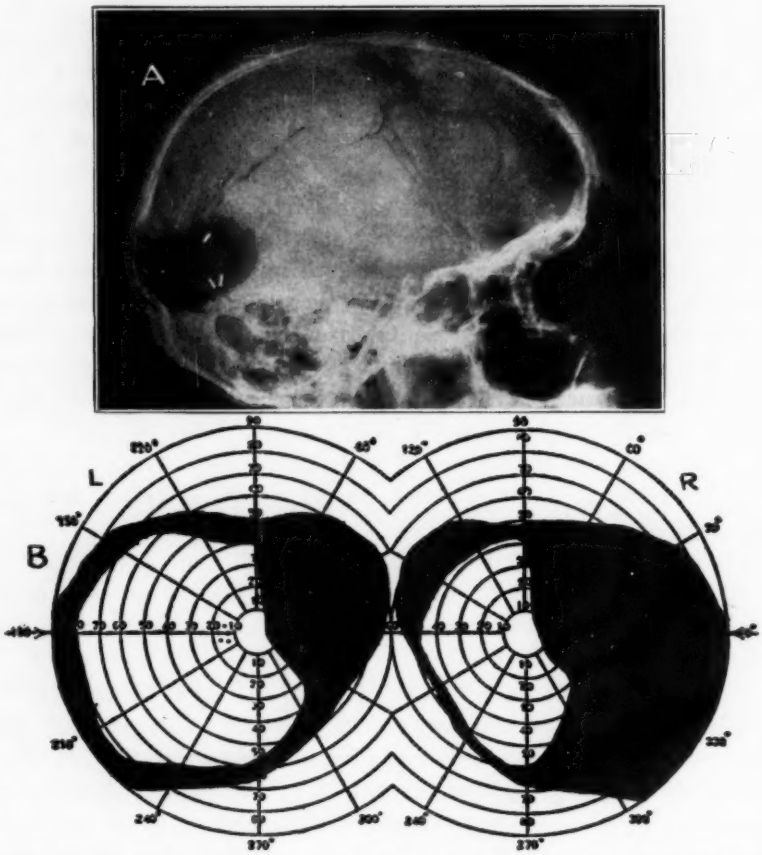


Fig. 1.—*A*, roentgenogram; *B*, visual fields taken with a 5 mm. white test object. Visual acuity: 20/15 in each eye.

In this figure, and in the accompanying figures, the visual fields are not plotted in the usual manner, owing to lack of proper cards at the time the charts were made. In some instances a card for the right eye was used for both eyes, but this should not detract from the reader's interpretation of the fields.

REPORT OF CASES

Case 1.—A white man aged 21 was wounded by a shell fragment Aug. 7, 1944, sustaining a fracture in the left parieto-occipital region of the skull, with multiple depressed fragments of bone, laceration of the dura and brain and intracerebral clot.

Two days later craniotomy was performed, with repair of the dura with fascia lata. Healing was uneventful except for some drainage of the cerebro-

spinal fluid for about four weeks. There remained a palpable depression at the site of the injury.

A roentgenogram of the skull showed an oval area of bony dehiscence, measuring 5 by 3 cm., in the posterior portion of the left parietal bone and the anterior portion of the left leaf of the occipital bone. Three metallic clips were visible in this defect. A metallic shadow and an indefinite calcified mass measuring 1.5 by 1 cm. were located 4 cm. medial to the center of the bony defect.

The field defect was right homonymous hemianopsia, congruous with sparing of the fixation area and sparing of a small portion of the lower portion of the right field adjacent to the midline. Vision was 20/15 in each eye, with ability to read Jaeger type 1.

Interpretation.—The site of injury, the data obtained at operation, the roentgenographic evidence and the field defect indicated a lesion of the left occipital cortex. Sparing of the fixation area was probably due to the dural blood supply by the calcarine artery and the middle cerebral artery. Another explanation always to be considered is fortuitous escape from injury of that portion of the area striata representing the fixation area, i. e., the posterior tip and the lateral surface of the occipital pole.

CASE 2.—A white man aged 24 was wounded by fragments of an 88 mm. shell on June 15, 1944, sustaining a compound, depressed fracture of the skull, with injury to the brain in the right temporoparietal area, a retained metallic foreign body in the left occipital lobe of the brain and complete hemianesthesia, with no loss of motor function.

On the day of injury the shell wound in the skull and brain was debrided; bleeding from the temporal artery, the middle meningeal artery, the temporo-occipital veins and the severed inferior petrosal sinus was arrested. Lacerated, contused dura and brain tissue from the temporal and occipital lobes was removed with suction. A graft of fascia lata was used to close the defect in the dura. Large sections of bone had to be removed in order to elevate the depressed fracture and to control bleeding. The patient was given 3,000 cc. of blood because of severe hemorrhage. No pulse or blood pressure was elicited for forty minutes. Five hours after operation the blood pressure was 120 systolic and 80 diastolic.

This soldier was unconscious from the time of injury until at least two weeks later, when he found he was totally blind, that he could move his left arm and leg, although he had no sense of position, and that he had loss of sensation over the left side of his body. There was no speech defect, and no personality changes were noted.

Roentgenographic examination showed an extensive comminuted fracture of the right temporoparietal area, with a large separated fragment in the upper occipital area. A metallic fragment measuring 5 by 4 mm. was present at the site of entrance, and a foreign body 10 by 15 mm. was present in the left occipital lobe. Roentgenographic examination on August 28 showed the following condition: "A large bony defect on the right side involved the posterior half of the parietal bone, the temporal bone, the upper margin of the mastoid and a small portion of the adjacent occipital bone, with two radiating linear fractures through the occipital bone. A metallic foreign body measuring 2.3 by 1.3 by 0.7 cm. was present in the left occipital lobe 1.5 cm. to the left of the midline and 1.5 cm. deep to the inner table."

Electroencephalographic examination showed an abnormal record indicative of damage to the right occipital and parietal areas.

On September 7 a tantalum plate measuring 11.5 by 11.5 by 14 cm. was inserted to cover the bony defect in the skull.

The field defect was left homonymous hemianopsia with division of the fixation area. Vision was limited to light perception in the right eye and was 2/200 in

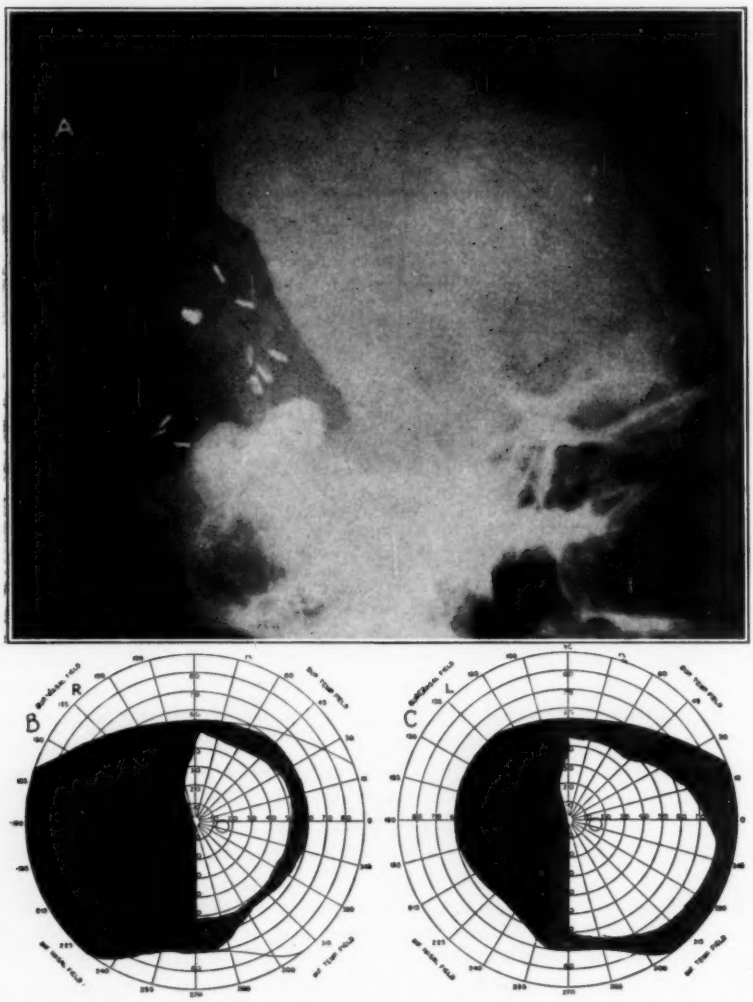


Fig. 2.—*A*, roentgenogram; *B* and *C*, visual fields of right and left eyes, respectively, taken Oct. 30, 1941 with a 15 mm. test object at a distance of 330 mm. Visual acuity: 1/200 in each eye.

the left eye. Reduction in vision may have been due in part to extensive hemorrhages in the vitreous of each eye. No lesions were visible in the fundus. There was no direct injury to either eye. The hemorrhages are to be explained by a

sudden increase in intracranial pressure and consequent compression of the vaginal space of the optic nerves and bleeding from the central veins.

Interpretation.—Injury to the right occipital and parietal lobes by penetration of a foreign body accounts for the left homonymous hemianopsia and left hemianesthesia and the mild left hemiplegia. The field

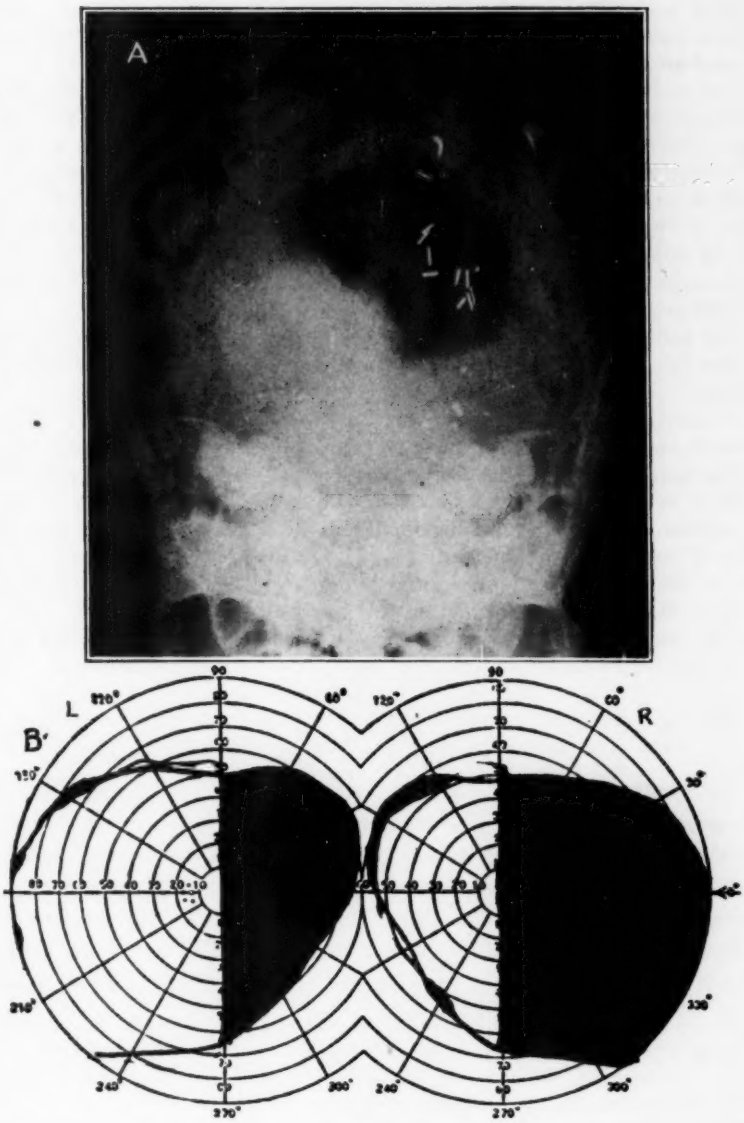


Fig. 3.—*A*, roentgenogram; *B*, visual fields taken with a 3 mm. white test object. Visual acuity: right eye, 20/70 — 1, with pinhole disk, 20/70 — 1; left eye, 20/200, with pinhole disk, 20/200.

defect was noted as early as Aug. 11, 1944 and has remained unchanged, although the hemorrhage in the vitreous has been largely absorbed. The foreign body in the left occipital lobe apparently did not damage the visual fibers or the cortex.

CASE 3.—A white man aged 23 was wounded by shell fragments Sept. 26, 1944, sustaining a severe compound, comminuted fracture of both leaves of the occipital bone, with extensive stellate fractures of both parietal bones; multiple metallic foreign bodies were seen at a depth of 5 to 6 cm. in the left parieto-occipital area.

The next day craniotomy was performed. Wide débridement, including removal of fragments of bone, was carried out, leaving a defect 6 by 3 cm. in the occipital bone. The dura to the left of the midline was torn, and there was a subdural hematoma. Damaged brain tissue and the hematoma were removed, and the track of the foreign body in the left occipital lobe was irrigated, but the foreign bodies were not removed. The dural defect was closed with a pericranial graft, and the defect in the scalp was closed with a sliding flap.

Examination prior to operation revealed no light perception in either eye, but both pupils reacted to light.

The patient remained apparently blind for fifteen days, when he was found to have light perception. He also exhibited sensory aphasia and generalized hyperreflexia.

Bilateral papilledema was present for a considerable length of time but subsided, leaving yellowish nerve heads with absence of physiologic cupping.

Roentgenographic examination of the skull showed a semilunar defect measuring 4 by 8 cm. in the occipital bone, the larger portion lying to the left of the midline. Linear fracture lines extended in all directions from this defect, and a Y-shaped fracture extended upward from the greater wing of the sphenoid bone on the right. Two large foreign bodies were present in the brain near the left parietal bone 9 cm. above the mastoid process.

The field defect was right homonymous hemianopsia with division of the fixation area. Visual acuity was as follows: right eye, 20/70 + 2; left eye 20/100 + 1, with correction. He read Jaeger type 12 with each eye, with correction. Degenerative changes secondary to prolonged papilledema were present in each macular area. This accounts for the poor visual acuity.

Interpretation.—The injury to the occipital region, with a tract of foreign bodies through the occipital and parietal lobes, together with the data obtained at operation, the roentgenographic evidence and the field defect, indicates damage to the left occipital cortex and the deeper tissue of the brain. The sensory aphasia and hyperreflexia indicate damage to the parietal lobes. In June 1945 vision was 20/50 —1 in each eye, with ability to read Jaeger type 9. There was no papilledema. The disk was still yellowish.

CASE 4.—A white man aged 29 was wounded by a high explosive shell July 11, 1944, sustaining a depressed, compound, comminuted fracture in the left parieto-occipital region with damage to the dura and brain.

The next day craniotomy was performed. Multiple depressed fragments of bone, hair, dirt and soft brain tissue were removed. The dural defect was repaired with pericranium.

There was a transient palsy of the sixth nerve. The pupils reacted to light. The fundi were normal.

Roentgenographic examination showed a debrided defect measuring 3.5 by 5.5 cm. in the superior right occipitoparietal region with radiating linear fracture lines

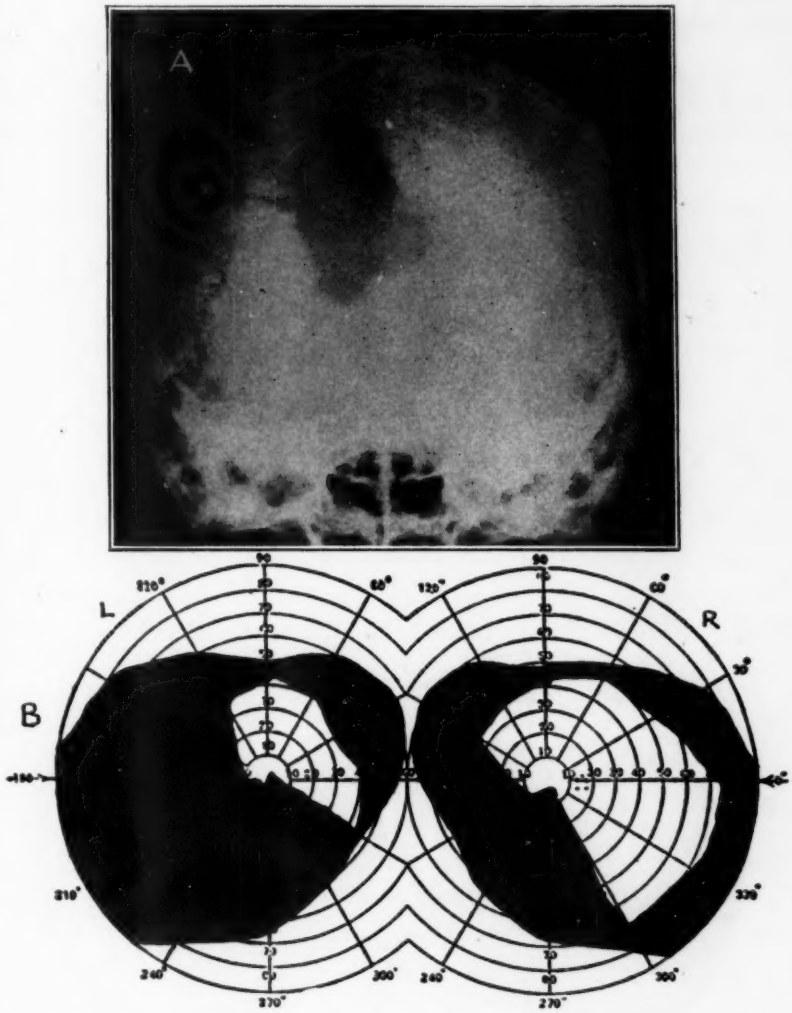


Fig. 4.—*A*, roentgenogram; *B*, visual fields taken Dec. 18, 1944 with a 5 mm. white test object. Visual acuity: right eye, 12/200; left eye, 2/200.

extending into the left and right lower occipital areas, into the right upper parietal area and along the lateral portion of the right parietal bone into the right temporal bone. Some partially detached fragments of bone lay in the left lateral portion of the bony defect. No intracranial foreign bodies were noted. The optic foramens showed no abnormality.

The field defect was left homonymous hemianopsia with considerable loss of the right lower quadrant of the field of each eye, especially in the left eye, and involvement of both fixation areas.

Visual acuity was 20/200 in the right eye and 6/200 in the left eye (eccentric), with ability to read Jaeger type 0.

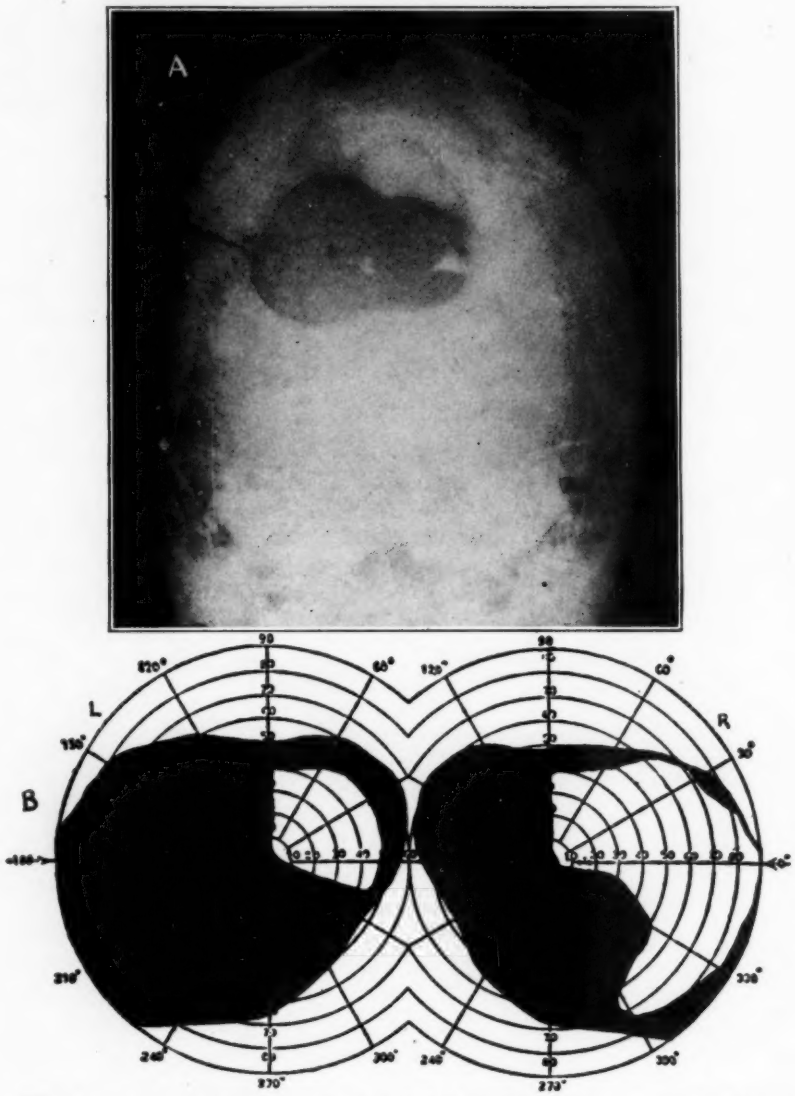


Fig. 5.—*A*, roentgenogram; *B*, visual fields taken with a 3 mm. white test object. Visual acuity: 8/200 in each eye.

Interpretation.—The site of injury and the data obtained at operation and by roentgenographic examination, together with the field defects,

indicate damage to the posterior pole of both occipital lobes, especially the right, and to the optic radiations on the left. The fields varied somewhat between December 18 and January 8.

CASE 5.—A white man aged 31 was wounded Aug. 8, 1944 by fragments of mortar shell, sustaining a compound, comminuted fracture of the occipital bone, more extensive to the right side of the midline, with depressed fragments of bone damaging the right occipital lobe.

Two days later craniotomy was performed. The tip of the occipital lobe and the calcarine area on the right side was reduced to pulp by deeply in-driven fragments of bone. The dura was torn on both sides of the midline. The longitudinal sinus was lacerated and thrombosed. Fragments of bone and pulped brain tissue were removed. The soldier was unconscious about eleven days.

Examination showed that he was completely blind for several days after this and later showed ability to count fingers and left homonymous hemianopsia on the confrontation test. The fundi were normal.

Roentgenographic examination showed an irregular defect measuring 1¾ by by 2½ inches (4.5 by 6 cm.) involving the occipital bone on each side of the midline, with a stellate fracture extending through the right parietal bone and terminating in the right frontal bone.

The field defect was left homonymous hemianopsia with involvement of both fixation areas and loss of a large portion of the right lower quadrant of the field.

Vision was limited to counting of fingers at 3 feet (90 cm.) in the right eye and at 4 feet (120 cm.) in the left eye. He read Jaeger type 0 with each eye.

Interpretation.—The left homonymous hemianopsia was due to damage to the right calcarine area. The damaged area in the left occipital cortex must have lain above the calcarine fissure and involved the tip of the posterior pole to produce a lower field defect with loss of the fixation area.

CASE 6.—A white man aged 19 was wounded by a sniper's bullet May 18, 1943, sustaining a gutter type of wound 1 by 3 inches (2.5 by 7.5 cm.) in size in the posterior portion of the parietal bones and the superior portion of the occipital bone, chiefly to the left of the midline, with in-driven fragments of bone. Brain tissue was herniated through an infected wound, through which cerebrospinal fluid was draining. Closure of the scalp wound could not be done until June 16, when pinch grafts were used to cover the defect, after the infection had been controlled. Pupillary reaction to light was normal. The fundi were normal.

A roentgenographic examination revealed a gross defect involving the posterior aspect of both parietal bones and the superior portion of the occipital bone, with metallic foreign bodies and fragments of dead bone lying in the brain substance.

The fracture lay chiefly to the left of the midline, with a linear fracture extending into the left parietal bone.

The field defect was complete right homonymous hemianopsia with loss of about one-half the lower left field of each eye and involvement of both fixation areas. There was also loss of the temporal periphery of the temporal field in the left eye.

Vision was limited to perception of hand movements in the nasal quadrants of the right eye and in the temporal quadrants of the left eye.

Interpretation.—The location of the defect in the skull and the field defect indicate damage to the left occipital cortex with less extensive damage to the right cortex at the posterior pole and above the level of the calcarine fissure, producing the defect in the left lower fields and involvement of the fixation areas.

CASE 7.—A white man aged 26 was wounded April 29, 1944 by shell fragments, sustaining a compound, comminuted fracture of the right parietal region,

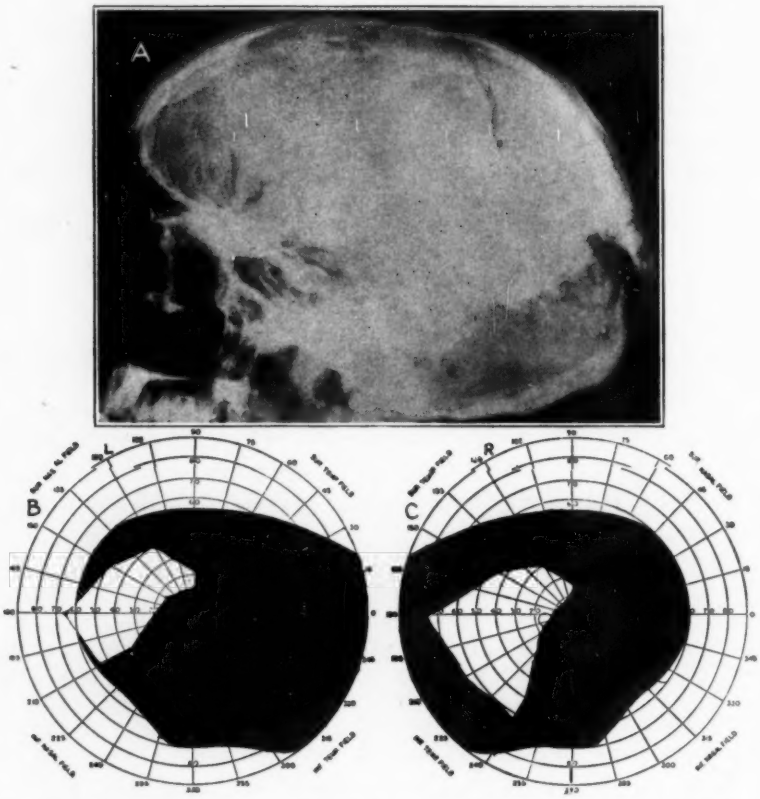


Fig. 6.—*A*, roentgenogram; *B* and *C*, visual fields of the right and left eyes, respectively, taken Jan. 8, 1944 with a 15 mm. test object. Vision was limited to light perception in each eye.

with herniation of brain substance from the wound. The patient was totally irrational and had complete flaccid left hemiplegia.

The following day a craniotomy was performed. Devitalized brain tissue was debrided, and the wounds were closed primarily. This had to be repeated seven days later, owing to a new herniation of brain tissue. A third craniotomy was performed because of a deep-seated abscess in the posterior parietal area. After this the patient showed notable improvement and became rational and

cooperative for the first time. Massive intraocular hemorrhages, without evidence of direct trauma to the eyes, had been noted. The patient was said to be entirely blind. He showed pronounced variations in mood.

Roentgenographic examination showed an area of bony dehiscence in the mid-portion of the right parietal bone adjacent to the sagittal suture and measuring

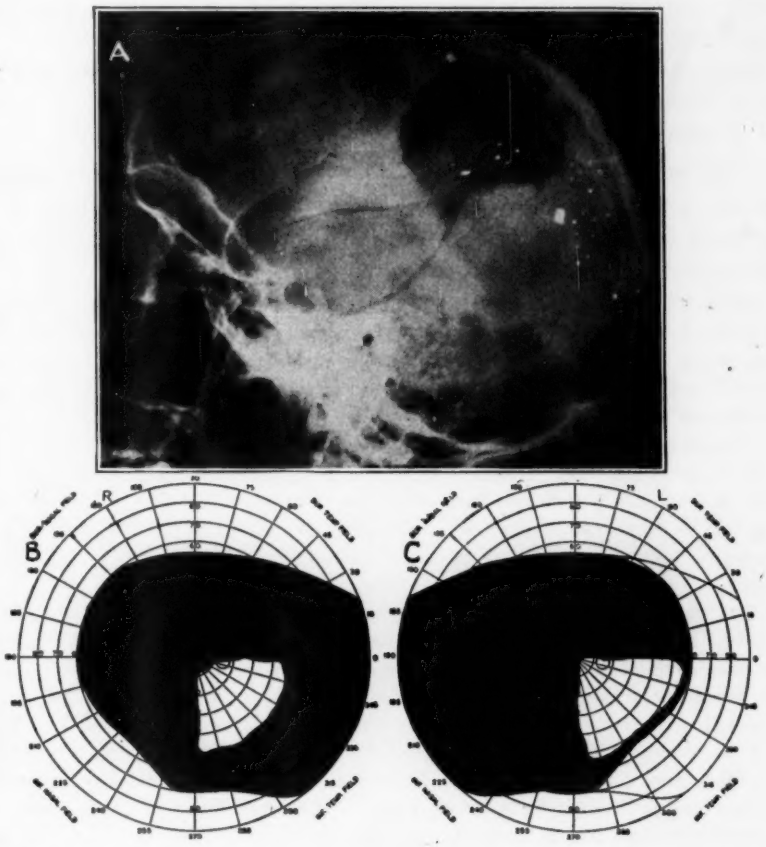


Fig. 7.—*A*, roentgenogram; *B* and *C*, visual fields of right and left eyes, respectively, taken Oct. 28, 1944 with an ophthalmoscopic bulb test object. Vision was limited to perception of hand movements at 1 foot (30 cm.).

6 cm. in diameter. Two linear depressed fractures extended downward and upward from this defect into the base of the skull.

The field defect was loss of all but a portion of the right lower fields of vision, with loss of both fixation areas.

Vision was limited to perception of hand movements at 1 foot (30 cm.) in each eye.

Interpretation.—Bilateral injury to the occipital lobe, greater on the right side, with damage above the level of the calcarine fissure

would explain the field defect. Observations at operation did not include examination of the occipital lobes.

A diagnosis of penetrating wound of the right frontoparietal region with a tract of numerous small metallic foreign bodies extending from this area through the right parietal lobe into the left occipital lobe was made overseas. Only widespread injury to the right optic radiations (including the macular fibers) and damage to the left occipital lobe can explain the defect on this basis, and there is lacking sufficient evidence in the record to justify such a statement.

A contrecoup injury to both occipital lobes is a possibility.

The hemorrhages in the vitreous without evidence of direct injury to the eyes may be explained by sudden increase in intracranial pressure with consequent pressure on the vaginal sheath of both optic nerves and hemorrhage from the central vein.

CASE 8.—A white man aged 34 was wounded March 25, 1944 by fragments of artillery shell, sustaining an H-shaped, compound, comminuted, depressed fracture of the skull in the midoccipital region just above the lambdoid suture and several deeply placed metallic foreign bodies. Four were near the midline, and one was in the right occipital lobe.

Craniotomy was performed on the day of injury. A laceration of the dura of 2 cm. over the right occipital lobe with a tract extending 6 cm. anterolaterally into the occipital lobe was found. The tract was debrided and a foreign body removed from the end of the tract with a magnet. A depressed fragment of bone measuring 3 cm. was removed, revealing a laceration of the superior longitudinal sinus.

The patient was at first conscious, rational and oriented. He complained of complete blindness. The pupillary reactions and extraocular muscles were normal. On May 28 there developed stertorous breathing and loss of all muscle tone. Lumbar puncture revealed fresh bloody fluid under increased pressure. The patient gradually improved. On April 12 ventriculographic examination was performed, bilateral trephine openings being made in the posterior parietal region. The lateral ventricles were dilated, and there was asymmetry of the occipital horns, the left failing to fill with air. On April 17 a second craniotomy was done. Débridement of necrotic tissue left a cavity 5 by 3 cm. in size. When the right ventricle was punctured, the brain began to pulsate for the first time. A second tract was found running parallel to the right occipital horn, 1.5 cm. wide and about 8 cm. deep. It was felt that a hemorrhage had occurred into the ventricle and that this accounted for damage to the third nerve at the aqueduct.

Roentgenographic examination showed a large, irregular defect in the midline of the skull, involving the superior portion of the occipital and the posterior portion of the parietal bone. A small metallic foreign body lay 2 cm. to the right of the midline, deep to the superior border of the defect. The optic foramens showed no evidence of fracture.

The field defect was loss of all the field of each eye except for retention of 2 degrees in each fixation area. Vision was nil for a long time after injury. On June 18 it was unimproved and was limited to light perception in each eye. He read Jaeger type 0 with the right eye and Jaeger type 3 with the left eye.

On Jan. 18, 1945 vision had improved to 20/50 + 1 in the right eye and to 20/20 — 2 in the left eye. He read Jaeger type 2 with each eye, with correction for the left eye.

Interpretation.—Bilateral homonymous hemianopsia with sparing of both fixation areas indicated a lesion in both occipital lobes without destruction of the tip of either occipital lobe, where macular vision is represented in the cortex. This case is the antithesis of case 11 (J. H.), in which bilateral central scotomas with normal peripheral fields were

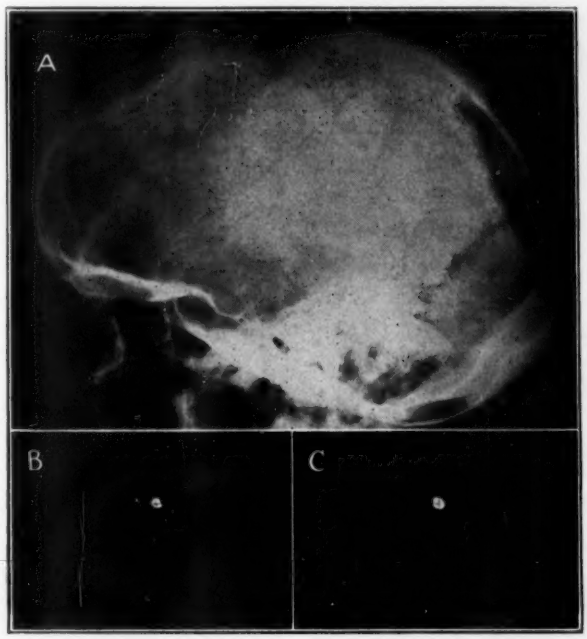


Fig. 8.—*A*, roentgenogram; *B* and *C*, tangent screen charts for right and left eyes, respectively, taken with 3 mm. white test object at distance of 60 inches (1.5 meters). Visual acuity: right eye, 20/100 + 1, corrected to 20/50, with ability to read Jaeger type 2; left eye, 20/30, corrected to 20/20 — 1, with ability to read Jaeger type 1.

found. The exact extent of damage to the optic radiations could not be told. Improvement in vision is accounted for by subsidence of edema in the occipital areas.

Case 9.—A white man aged 26 was wounded March 4, 1944 by fragments of an artillery shell, sustaining a compound, depressed fracture of the left leaf of the occipital bone and several foreign bodies in the left frontal lobe.

Craniotomy was done on the day of injury. This consisted of débridement of the wound in the left occipital lobe, packing of the longitudinal sinus with muscle tissue and closure, with drain in place.

On March 11 he was found to be completely blind, although both pupils reacted to light. There was bilateral papilledema.

On March 12 a second craniotomy was done, with evacuation of a subdural hematoma which was compressing the left hemisphere about 1.5 cm. The left occipital lobe was badly damaged, and the necrotic tissue was removed. A defect 3 cm. deep was left. After this, a clot was removed from over the right occipital lobe, the cortex of which was completely liquefied. The neurosurgeon's operative note states: "There was considerable damage to both occipital lobes, thus accounting for blindness. The damage, however, did not appear to me to destroy the the calcarine area completely, and it may be that after edema subsides some vision may return, particularly in the upper fields."

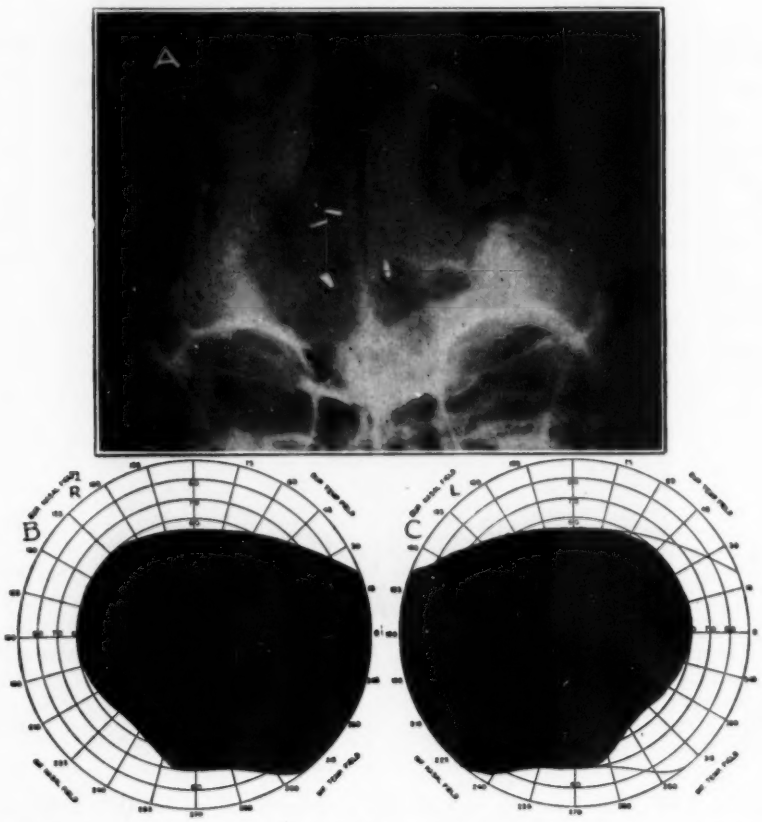


Fig. 9.—*A*, roentgenogram; *B* and *C*, visual fields of the right and left eyes, respectively, taken Oct. 30, 1944, with a 5 mm. test object at a distance of 330 mm. Visual acuity: 20/40 in the right eye; 20/20 in the left eye.

By March 23 the patient had light perception. When first seen, he could tell time on a wall clock 10 feet (3 meters) away.

On November 16 vision was 20/40 + 1 in the right eye and 20/20 in the left eye; he read Jaeger type 6 with the right eye and Jaeger type 1 with the left eye.

Roentgenographic examination showed a bony defect measuring 6 cm. in diameter in the left postparietal area with radiating fracture lines extending anteriorly.

The field defect was loss of all field in each eye except for retention of 1 degree in the fixation area. The patient was able to read only one letter at a time, but this he saw quite clearly, both for distance and for near vision.

Interpretation.—There was damage to both occipital lobes, with fortunate sparing of the cortical areas representing the fixation area of the retina. Damage to the anterior portion of the calcarine area accounts for loss of the peripheral field. The fixation area of the cortex of each side must have been preserved. The neurosurgeon felt that the entire cortex had not been destroyed. The radiations are undoubtedly damaged in such injuries as those pointed out by Holmes.

CASE 10.—A white man aged 23 was injured in a plane crash July 15, 1943, sustaining a compound, depressed fracture in the midoccipital region of the skull with contusion of the right occipital lobe.

Thirty-six hours after the injury a craniotomy was performed to elevate the depressed fracture. The edges of the skin were debrided down to the periosteum; two fragments just to the right of the torcula, 3 by 1 cm., found driven inward 1.5 cm. and piercing the longitudinal sinus, were pried up and removed. Bleeding was arrested. The right portion of the occipital bone, which had been bent inward, was pried outward. The dura was intact and pulsating freely; it was not opened. The scalp was closed with one layer of interrupted steel sutures. An occipital defect in the skull, about 2 by ¾ inch (5 by 1.9 cm.), was repaired with a tantalum plate on Jan. 10, 1944.

A roentgenogram of the skull revealed a large, irregular defect in the posterior aspect, beginning approximately 4 cm. above the lambdoid suture and extending into the occipital bone approximately 4 cm. The defect involved chiefly the right side.

The field defect on Aug. 13, 1943 was left homonymous hemianopsia with sparing of the fixation area. On Dec. 13, 1943 the field defect was left homonymous lower quadrantanopsia with the fixation spared. Vision on the earlier date was 20/30 in each eye, with ability to read Jaeger type 1. On the latter date vision was 20/15 in the right eye and 20/20 in the left eye. He read Jaeger type 1 with each eye.

Interpretation.—The left homonymous hemianopsia is explained by damage to the right occipital cortex.

The improvement in the field on second examination, four months later, can be explained on the basis of subsidence of edema in the area adjacent to the destroyed cortex.

CASE 11.—A white man aged 22 was wounded by fragments of shrapnel March 27, 1943, sustaining injury to the occipital region. Blindness immediately followed the injury. The patient became unconscious about twenty minutes later.

The following day a débridement was performed, and three days later vision began to return. There was gradual improvement in vision until some time in May, after which it remained stationary.

On August 2 the depressed fracture of the skull was elevated and numerous bony fragments and pieces of shrapnel were removed. Bony and metallic fragments were removed from the brain tissue in the right occipital pole, and the dura was opened on both sides of the longitudinal sinus. One bony fragment which entered the longitudinal sinus was left in situ, as an attempt to remove it resulted in severe bleeding. Both occipital lobes were found to be grossly

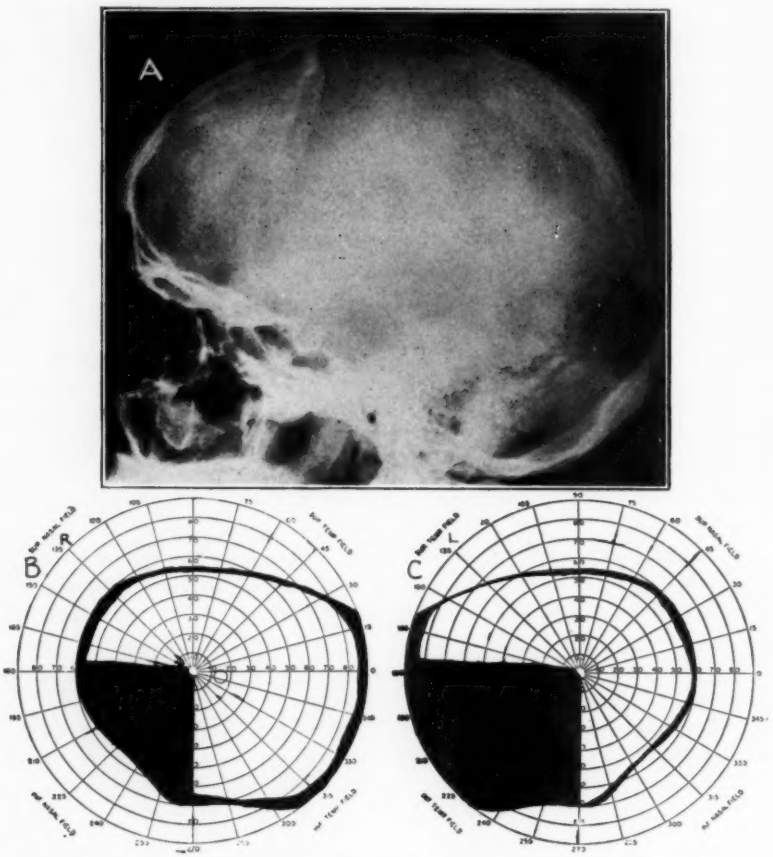


Fig. 10.—*A*, roentgenogram; *B* and *C*, visual fields of the right and left eyes, respectively, taken Dec. 13, 1943, with a 3 mm. test object. Visual acuity: right eye, 20/15; left eye, 20/20.

contused and degenerated, being represented by amorphous xanthomatous scarred cortex. This was freed as well as possible from the dura but appeared to be far beyond any hope of return of function.

On September 24 a tantalum plate was placed in the defect in the skull in the occipital region.

Roentgenographic examination of the skull showed a large defect in the midline of the occipital bone, the lower border being just above the inion. The defect was covered with a metallic plate.

The field defect was a large absolute homonymous hemianoptic scotoma. Vision was 20/200, eccentric, in each eye.

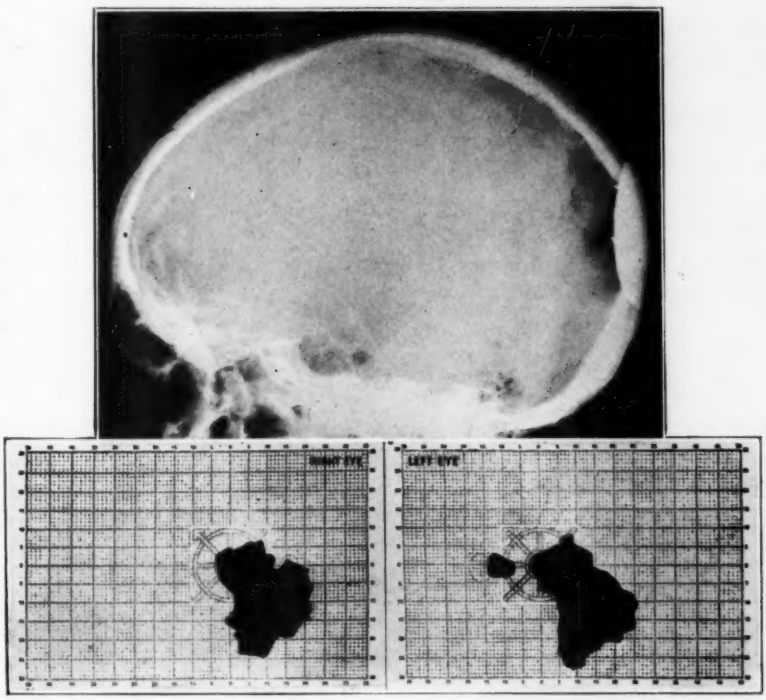


Fig. 11.—Above, roentgenogram; below, campimetric charts taken Nov. 27, 1943, showing absolute scotoma and right homonymous paracentral scotoma.

Interpretation.—The lesions indicate damage only to the posterior tip of the cortex of each occipital lobe, which was slightly more extensive on the left side.

CASE 12.—A white man aged 25 was wounded by an artillery shell fragment March 6, 1944, sustaining a blunt, nonpenetrating blow in the left frontal region.

Two days later it was noted that the right pupil was smaller than the left; both reacted sluggishly to light. Vision was poor in the right eye, and bitemporal hemianopsia was demonstrated. There was paresis of the right sixth nerve. Neurologic examination revealed nothing else of significance.

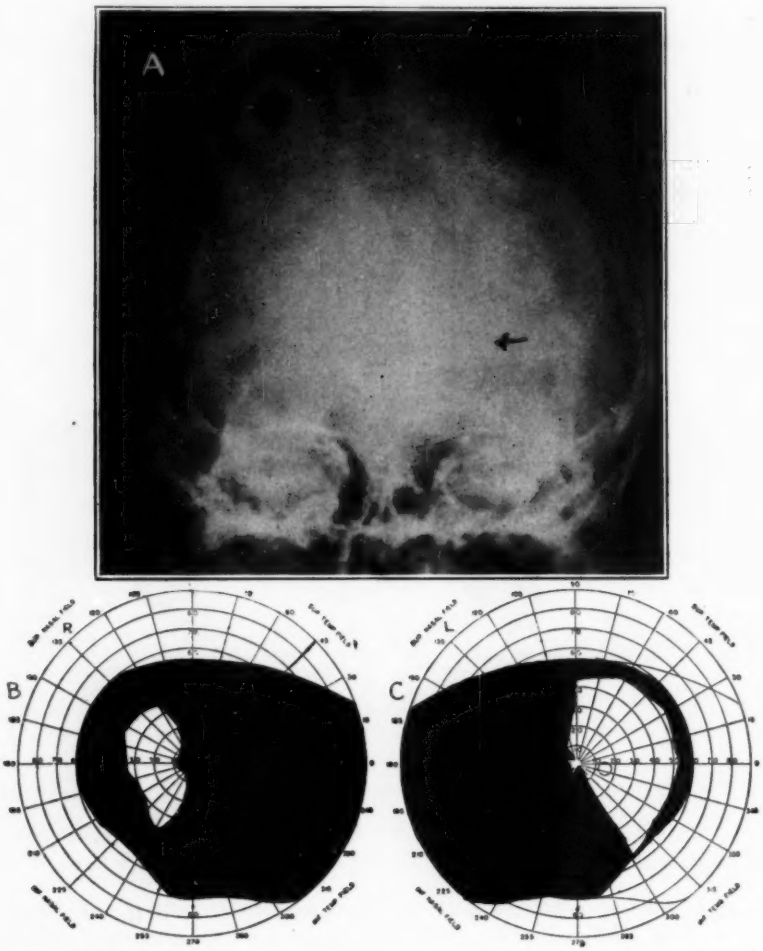
No operation was performed.

Roentgenographic examination showed a fracture in the left side of the frontal bone, beginning at the superior marginal rim of the orbit and extending upward

and outward toward the midline. The anterior table of the left frontal sinus was involved.

The fracture extended along the floor of the anterior fossa.

The field defect as noted on May 8, 1944 was a cleancut bitemporal hemianopsia. On September 10 the right eye showed loss of the entire temporal field, loss of the fixation area and the outer 15 degrees of the nasal periphery. The fixation area was involved. The left eye showed loss of the entire temporal



12.—*A*, roentgenogram; *B* and *C*, visual fields of the right and left eyes, respectively, taken with a 15 mm. test object on Oct. 9, 1944. Visual acuity: right eye, 1/200, eccentric; left eye, 20/20.

field except for a small area bordering the midline above the fixation area, which was not involved.

Vision was 1/200 (eccentric) in the right eye and 20/20 in the left eye. He read Jaeger type 0 with the right eye and Jaeger type 1 with the left eye.

The right nerve head was pale, and the lamina cribrosa was clearly seen. The left nerve head showed only a suggestion of pallor. The retinal arterioles were moderately attenuated.

Interpretation.—The lesion must have been located in the chiasm, involving principally the midportion, with damage to the crossed fibers and sparing of most of the uncrossed fibers. The first field examination showed cleancut bitemporal hemianopsia, but later a defect was found in the peripheral portion of the right nasal field. Vision in the right eye was affected almost immediately after the injury.

In 1935 Traquair, Dott and Russell [13] collected from the literature reports of only 27 cases of lesions of the optic chiasm and added 3 cases. In 2 of these 3 cases the defect was pure bitemporal hemianopsia; in the third case there were blindness in the right eye and a defect involving less than the entire temporal field of the left eye. Even in the first 2 cases central vision was reduced in one eye. Injury was usually to the frontal area and was due to a blunt blow. No fracture was found on rontgenographic examination in 6 cases. The sixth nerve was injured in 7 out of 30 cases. In 7 cases one eye was blind. The olfactory nerve was injured in 5 cases. In 7 cases polyuria was present, although it was transient in 2 cases. Traquair and his associates attributed the chiasmal damage to vascular lesions rather than to sagittal tearing of the chiasm.

Osterberg [14] reported 2 cases, with description of experimental studies on tearing of the chiasm in vitro. He was able to demonstrate multiple small tears and expressed the belief that the blood supply to the center of the chiasm was not separate from the supply to the lateral portions and that therefore the crossed fibers alone would not be affected by damage to blood vessels. Osterberg cited Coppez,[15] who demonstrated multiple minute tears in the crossed fiber bundles. He found that separation of the optic foramens a distance of 1.2 mm. by frontally applied force would produce tears because the optic nerves were firmly adherent to the foramens.

Henderson and Rucker [16] were able to show tearing of the chiasm in 1 case.

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13. Traquair, H. M.; Dott, N. M., and Russell, W. R.: Traumatic Lesions of the Optic Chiasma, Brain **58**:398 (Sept.) 1935.

14. Osterberg, G.: Traumatic Bitemporal Hemianopsia, Acta ophth. **16**:466, 1938.

15. Coppez, H.: Le mécanisme des lésions du chiasma dans les fractures du crane, Arch. d'opht. **46**:705-716 (Dec.) 1929.

16. Henderson, J. V., and Rucker, C. W.: Bitemporal Hemianopia of Traumatic Origin, Arch. Ophth. **24**:800 (Oct.) 1940.

Burch [17] recorded a case in which a fracture of the sella turcica resulted in bitemporal hemianopsia; vision was 20/25 in the right eye and was limited to ability to count fingers at 6 inches (15 cm.) in the left eye.

It is evident, therefore, that tearing does occur although damage to the blood supply must be considered as at least a contributory cause.

CONCLUSIONS

1. Correlation of visual field defects with definitely known sites and types of head injury, the lesions found at operation and the results of roentgenographic examination of the skull offers the best method of studying the cortical representation of various areas of the retina.

2. Cortical representation of the fixation area (macula) is similar to cortical representation of the peripheral portions of the retina. The fixation area is represented at the posterior tip of the occipital lobes, while the peripheral portions of the retina are represented in the cortex at the anterior end of the calcarine fissure. Intermediate points of the retina are represented between these two areas of the area striata.

3. Similarly, the upper half of the retina is represented in the cortex above the level of the calcarine fissure, while the lower half of the retina is represented below the calcarine fissure.

4. Neither the fixation area (macula) nor the peripheral area of the retina has duplicate areas of representation.

5. It follows, therefore, that homonymous hemianopsia, vertical hemianopsia and quadrantanopsia can occur in the peripheral field and that the central fields may also show homonymous scotomas, which may be lateral or vertical, central or paracentral, hemianopic or quadrantic. Combinations of homonymous hemianopsia and central scotoma also occur when missiles producing oblique wounds pass through the tip of one occipital lobe and through the occipital lobe or the optic radiations on the opposite side, as shown by Holmes and Lister.

6. Bilateral homonymous hemianopsia with sparing of the fixation areas (cases 8 and 9) represents the antithesis of bilateral central scotoma with normal peripheral fields. These cases support some of the statements in previously expressed conclusions.

7. Bitemporal hemianopsia can occur from damage to the chiasm, although it is rarely a "pure" hemianopsia. The mechanism of this damage to the uncrossed fibers alone is not entirely clear.

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17. Burch, F. E.: Ocular Evidence of Head Trauma, Wisconsin M. J. **41**: 1092, 1942.

PLASTIC REPAIR OF DEFORMITIES OF THE SOCKET AND MINOR DEFECTS ABOUT THE ORBIT

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THE ANATOMY of the socket deserves a clearer presentation than the anatomy of this region usually receives. "Socket" means the bed or receptacle of the prosthesis. Theoretically, consideration of the anatomy of the region should be simple, since its spatial relationships have been covered in great detail. Actually, the anatomy, and more particularly the physiology, of the orbit without the eye departs farther from the normal than study of the literature would lead one to think. The ratio of the volume of the globe to that of the orbit, according to Duke-Elder, is 4.5 : 1, but the removal of the one part makes a profound difference in the other.

There are essentially four types of sockets, depending on the procedure or the series of procedures by which the eye is removed. A separate discussion of each type, although elementary, may be advisable.

1. Socket formed by enucleation of the globe without an implant sphere, the procedure consisting of suturing together of the extraocular muscles and Tenon's capsule and covering with conjunctiva. This operation is the simplest and gives a fairly satisfactory base for a prosthesis. Movement is generally adequate, the method giving approximately a 10 degree range of movement of the prosthesis vertically and horizontally. Its principal disadvantage is that alteration in function causes atrophy of the orbital contents, which results in poor movement of the prosthesis. This point will be discussed later.

2. Socket formed by enucleation of the globe with an implant sphere placed in the cavity created by removal of the globe. Retention is obtained by suturing Tenon's capsule and the muscles together and covering with conjunctiva. The implant sphere may consist of any acceptable material—glass, tantalum, gold, plastic or preserved cartilage. We have had several bad results with implant spheres of bone, which have had a tendency to undergo necrosis, resulting in a foul orbital discharge and necessitating removal of the implant, with almost no hope of implanting another sphere because of the large amount of scar and fibrous tissue which forms around the bone in this area. This type of

socket gives better movement of the prosthesis than does the type previously discussed. The size of the implant should approximate the normal to give the best movement. If the implant sphere is too small, the purpose to give better mobility of the prosthesis will be defeated, and the implant will be no better than none at all. If it is too large, fitting an acceptable prosthesis is difficult, and Tenon's capsule may slip back from the sphere, leaving it thinly covered and vulnerable. Thus, the preparation of this type of socket in children is a poor choice, because the sphere is necessarily of limited size and in later years it shifts in the socket, making almost impossible the fitting of a prosthesis which is realistic in appearance and movement.

3. Socket formed by evisceration of the global contents, removal of the cornea, closure of the sclera without an implant and coverage with conjunctiva. The surgical indications and contraindications for this procedure are well covered in the literature and have no place in this discussion, which is concerned principally with results. From the point of view of the mobility and appearance of the prosthesis, the socket prepared in this way is much better than the two previously discussed. The prosthesis generally moves better horizontally and vertically, and there is also retained more than a suggestion of the action of the oblique muscles, since they are still intact. In our experience, the sockets which were prepared in this way when the patients were children had better beds for the reception of a good prosthesis in adult life than those formed by enucleation, either with or without implant.

4. Socket formed by evisceration of the ocular contents with an implant sphere placed in the scleral sac, followed by closure of the sclera and conjunctiva. This procedure undoubtedly gave the best results. Movement of the prosthesis was 50 per cent normal or better both vertically and horizontally. The amount of late atrophy was about the same as that in the third type of socket and was much less than with enucleation.

The changes which occur from removal of the eyeball until the death of the patient are fairly progressive and account for the further variety of sockets which we have seen.

The bony walls of the orbit are usually unchanged in the removal of the eye, although when they are altered, as in battle casualties, additional problems are presented. Normally, the lateral wall of the orbit is the strongest, especially where the frontal bone joins the great wing of the sphenoid bone and the zygomatic bone. At this point the margin is curved backward so that the visual field may be wide laterally, and there are almost no structures of the bony walls to interfere with this function. The orbital tubercle is at about the middle of the lateral wall, and to it is attached the lateral retinaculum. From this point up to the

site of insertion of the combined tendon of the superior rectus and the levator palpebrae superioris muscle there is almost no integral attachment between wall and contents, as there is in the other quadrants of the orbit. It is for this reason that no structure holds the implant there. Considerable atrophy of orbital fat is seen to a greater or less degree in all sockets with which we have come in contact, and this apparently was the original experience of Snell, since the prostheses generally have their greatest area in this location. Associated with this atrophy, as with all other changes in the socket, is the factor of gravity. The check ligaments of unused muscles and the muscles themselves become soft and tend to fall to the floor of the orbit when the edema and hemorrhage associated with the operation are absorbed and replaced with fibrous tissue over the years. In most sockets which we have examined fifteen or twenty years after the operation there is a redundant mass of tissue at the floor of the orbit, making the fitting of a prosthesis which is lifelike a difficult task.

Associated with the alteration in function in the socket, various changes occur in the conjunctiva. These changes begin almost as soon as removal of the eye is finished and are usually more profound than is generally indicated. For example, in a case of evisceration in which the cornea is removed, the loss of tissue, necessitating coverage by the conjunctiva, is usually compensated for by decrease in size of the globe. Normally the conjunctiva is more than ample and folds into the fornices. However, when the associated edema and hemorrhage have subsided, the conjunctiva loses its normal elasticity by replacement of elastic fibers with fibrous tissue. It becomes thickened and resistant, like a rubber band which after being on stretch is suddenly relaxed. This change occurs in the orbital, fornical, bulbar and limbal conjunctival areas. The changes are modified somewhat by the type of operation and by the length of time that elapses between the operation and the insertion of a conformer or prosthesis. We have seen a number of cases in which the time which elapsed after operation was as long as twenty years. In such cases the conjunctiva is firm and fibrous and the lower fornix, or sulcus, is entirely absent, so that one of the separative procedures must be carried out.

Grossly, the conjunctiva of the eye is considered as consisting of four portions: The palpebral portion, made up of marginal, tarsal and orbital conjunctiva; the conjunctiva of the fornix; the bulbar portion, consisting of scleral and limbal conjunctiva, and the plica semilunaris. Microscopically, the conjunctiva is made up of an epithelial layer and a substantia propria, consisting of an adenoid and a fibrous layer. The deeper, fibrous, layer is a thick collection of collagenous and elastic fibers. It is absent over the tarsal region but begins at the edge of the tarsus and extends back over the orbital portion of the conjunctiva of

the globe. It is reenforced by the insertion of the levator in the upper fornix, and we feel that this reenforcement is the reason that fewer changes are seen in the upper portion after operation. The change takes place in the substantia propria of the conjunctiva, most likely in the elastic fibers of the fibrous layer.

Within the upper lid are two potential spaces, separated by the aponeurosis of the levator muscle. Both these spaces are lost and the lids are profoundly involved in the metamorphosis of the structures. The changes in the eyelids are much greater on their external surfaces. The superior orbitopalpebral sulcus is deepened, and the inferior orbitopalpebral sulcus tends to be obliterated. The fornices, as we have noted before, are lost, and the fibers of the orbicularis muscle become relaxed and redundant. This is especially true inferiorly. One of the operations to be described later is helpful in repair of this condition. The elasticity of the lids is not lost to the extent that it is in the conjunctiva, and the changes seem largely innervational, or trophic. It is felt that the change is in the septum orbitale, since the most profound effect is in the lower lid, where this septum is complete. In the upper lid, where the septum blends with the levator muscle, the changes are not so pronounced.

To summarize: It is felt that after removal of the visual mechanism there are certain uniform changes in the eyelids, muscles, conjunctiva and socket which are in the nature of atrophy; that these changes proceed along fairly uniform lines, although their progression may be altered substantially by early and well fitting prostheses, and that once they are well established the only effective treatment is with the operative procedures to be discussed.

OPERATIVE PROCEDURES

Various modifications of procedures for correction of contracted socket with free skin grafts have been presented in the literature.[1] Wheeler [2] has practically standardized the technic of operation, but a few problems encountered in large scale repair at ophthalmic centers should, we feel, be taken into consideration when deviations from standardized procedures become necessary.

We do not believe that Wheeler and others intended to standardize a procedure which was to be used in every case of contracted socket.

1. Kilner, T. P.: The Application of the Thiersch Graft to Special Areas, Post-Grad. M. J. **10**:317, 1934. Spaeth, E. B.: Principles and Practice of Ophthalmic Surgery, ed. 2, Philadelphia, Lea & Febiger, 1941. Sheehan, J. E.: Plastic Surgery of the Orbit, New York, The Macmillan Company, 1927.

2. Wheeler, J. M., cited by Spaeth, E. B.: A Review of Some Modern Methods for Ophthalmic Plastic Surgery, Am. J. Surg. **42**:89, 1938; Use of Epidermic Graft in Plastic Eye Surgery, Internat. Clin. **3**:292, 1922.

There are many variations in deformities of the socket, and these should receive much more consideration than they have in the past and their repair planned accordingly. The terms "never" and "always" should not apply in this type of reconstruction, since so much good is done by procedures which may have been condemned by some surgeons but have served a good purpose in the hands of others. Repair of the socket, in our opinion, deserves as much consideration as any other form of repair about the orbit and face. On a well planned repair will depend the

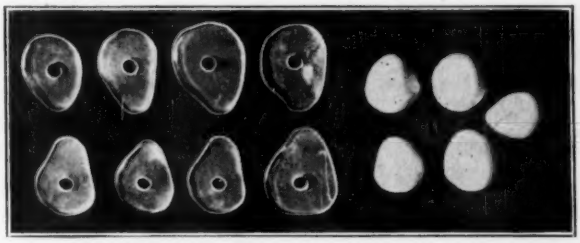

Fig. 1.—Different types of acrylic conformers used in eye sockets after various grafting procedures, as illustrated in the text. The clear acrylic type is usually inserted after the stent or rubber mold is removed. The others were made according to the size and shape of artificial eyes. Lately we have substituted clear acrylic plugs.

Fig. 2.—*A*, socket completely lined with skin. Notice the remnant of caruncle preserved. There is also a deformity of the left eyebrow, which was corrected by the Z plastic operation, as seen in *B* (operation performed with Major Sanders K. Stroud). *B*, result after insertion of artificial eye and correction of the deformity of the eyebrow.

satisfactory fitting of a prosthesis. In these circumstances, there cannot be a standardized method of repair.

With the advent of acrylic artificial eyes, patients are becoming much more eye conscious and are as much disturbed with a slight exophthalmos as with the notching of the lids or a misplaced eyebrow. This is just an example of what ophthalmic surgeons can expect on return to

civilian life, and they must be prepared to analyze the various contours of the orbit and to plan operative procedures accordingly, in order better to assist in the fitting of a prosthesis that will satisfy the patient.

Complete Lining of Socket with Skin.—We agree that there is little difficulty in the method of completely lining the socket with skin. When we consider the factor of movement, we are inclined to work out a definite plan for this procedure. Every patient desires as much movement as possible in the prosthesis. A completely skin-lined socket has a tendency to restrict movement in many cases, and in a socket requiring a complete lining, including both cul-de-sacs and the lids, we suggest grafting the lids and both cul-de-sacs first and leaving the central, movable, portion of the socket for a second stage procedure. We found that a line of demarcation at the junction of the movable-nonmovable portions of the socket adds greatly to the final movability of the fundus of the socket. This was brought to our attention in the repair of previously grafted sockets with absence of both cul-de-sacs. The graft in the central portion of the socket was left intact, and movement was decidedly increased. The contour of the socket was also greatly improved, and the fundus had the appearance and consistency of a previously inserted fat graft or other implant. We have found in the case of the greatly retracted socket that a flap for the central portion might be more desirable because of the frequent necessity of secondary incision and implantation of some material. In our series of complete linings no flap was necessary.

Fig. 3.—Result of lining the lids and the nonmovable portion of the socket with skin. The old graft in the central portion of the fundus was not disturbed. The central, movable, portion of the socket has the appearance of having a fat graft implanted. Notice the depth of both the superior and the inferior cul-de-sac.

Dental stent has been a favorite material for the grafting of these sockets, but to make a complete and satisfactory lining with stent a canthotomy is often necessary. Personally, we do not feel, as do some surgeons, that performing a canthotomy is malpractice, since it can easily

be repaired. However, in consideration of the principle of not producing any more incisions than necessary, we have adopted the use of the rubber pad, as illustrated by Hughes and others, thus producing contact with all surfaces without any widening of the palpebral fissure. The pad is readily inserted with the graft and readily removed. Latex pads are ideal, provided they have a flat and slightly concave surface posteriorly and a slight convexity anteriorly. Frequently a pad with more convexity posteriorly is indicated, since it will produce more pressure against the posterior portion of the socket to be lined. Ordinarily, orthopedic rubber padding is rather firm but serves the purpose when shaped properly. A hole is placed in the central portion for drainage.

Absence of Conjunctiva.—All scar tissue on the lids and in both cul-de-sacs and in the socket itself is excised. Thin lids are essential, and the tarsus of the lower lid should be hugged in the dissection. If possible, the dissection should be begun slightly below the margin of the lid; it is continued inferiorly along the floor of the orbit, externally beneath the skin to the lateral orbital rim and medially to the margin of the lacrimomaxillary junction, care being taken to stay behind the caruncle or the remnant of the caruncle. Any remaining tissue should be retained in this region so as at least to simulate a caruncle. A portion of scar tissue is better than nothing at all, from the standpoint both of the cosmetic effect and the fitting. One can do tattooing later, if necessary, and dissection is then continued superoposteriorly, care being taken to avoid the fibers of the levator palpebrae superioris. Inferiorly, laterally and medially the periosteum should be roughened or incised so that the graft will become readily adherent in these regions. The rubber pad is then shaped accordingly and inserted, care being taken that there is contact all around. If a stent mold is used, hot or cold, sterile water should be available, a canthotomy performed and the mold shaped accordingly. The inner side of the upper portion of the arm is usually the choice for the donor area. A thin split graft is removed from this region and applied on a wet towel, with the raw surface down. Petrolatum gauze, gauze soaked with saline solution and a cotton wool dressing are applied over the donor area. The previously prepared mold is then placed on the graft and the graft applied over the mold. Glue is not necessary, and in our experience a thin graft is desirable. This graft is punctured in the central portion so as to provide for drainage through the hole in the mold. The mold and the graft are then inserted into the socket, with the raw surface of the graft on the outside. The lids are then approximated with two silk sutures; petrolatum gauze strips are applied, with an eye pad and fluff gauze pressure dressing. The lid sutures are removed on the fifth day; the mold is removed on the seventh day, and the socket is flushed with boric acid. The mold is then reinserted. On

the ninth day the mold is removed and an acrylic form inserted, as illustrated (fig. 1). This acrylic form is fitted accordingly and has a hole in its center for irrigation and drainage. This form can be removed at weekly intervals for cleansing and should then be reinserted until the contracture period of the graft has passed, which is usually from six weeks to three months. A form in the shape of an artificial eye can then be inserted and worn for a time, while the patient awaits the fitting of a satisfactory prosthesis. The graft within the socket is important and should be cleansed daily, followed by the application of a lubricant. One should not be in too great a rush to insert a permanent prosthesis but should wait until the graft has softened and has approached maximum contraction.

In the two stage procedure, the same technic is followed, and the central portion is grafted as a separate entity. We suggest suturing the graft in place, with the ends left long, so that they can be tied over

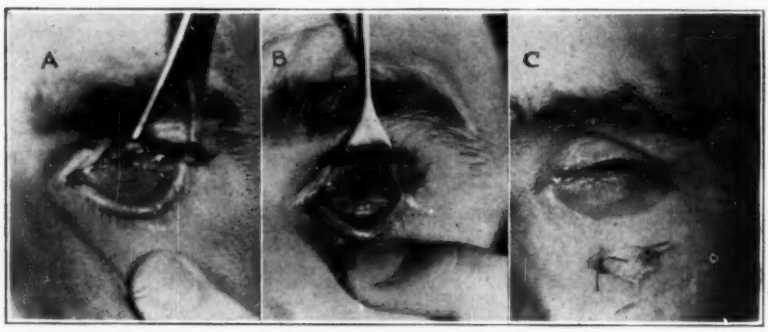

Fig. 4.—*A*, absence of the inferior cul-de-sac. The socket could not retain the artificial eye. The procedure outlined in the text was performed with a mucous membrane graft from the lower lip. *B*, result of procedure. A satisfactory cul-de-sac was produced. *C*, sutures tied over a piece of gauze on the cheek after insertion of a mucous membrane graft, as described in the text. A photograph of a different patient had to be shown for illustrative purposes, the sutures in the case shown in *A* and *B* having been removed before a photograph was available.

a fitted mold to provide pressure on the graft. Fluff gauze can be used for this purpose instead of a form-fitting mold.

Absence of the Inferior Cul-de-Sac.—This condition may be caused by lack of sufficient conjunctiva, cicatricial deformity or overabundance of conjunctiva, with the result that the artificial eye cannot rest properly and persists in slipping out. In cases of insufficient conjunctiva the mucous membrane graft is indicated. With local anesthesia, the socket-lid junction is determined and an incision made along this line. All scar tissue is excised. The incision is then extended down to the orbital floor, and care is taken to release all adhesions and attachments. Medially, the incision is extended in an oblique direction, to pass

laterally and beneath the caruncle. Laterally, it is extended to a few millimeters above the external canthus, assuming the appearance of a hammock. A small gauze strip is inserted to control bleeding. The inside of the lower lip is an ideal donor area. Sutures are inserted in the lower lip for traction purposes. With local anesthesia, the mucous membrane is ballooned out, and a full thickness graft is outlined and excised. The resulting raw area is repaired by direct approximation with a continuous suture of silk and interrupted sutures of silk. The graft is then transferred to the raw area of the cul-de-sac and sutured in place with fine silk. Interrupted sutures, with the ends left long, are inserted at intervals. The most important part of this procedure is the insertion medially and laterally of a stay suture of silk, entering through the graft and passing through the periosteum of the infraorbital rim and then out through the cheek. A piece of petrolatum gauze is placed within the socket between the loops of the sutures on top of the graft and the ends tied without over a piece of petrolatum gauze. This procedure assures one of a permanent sulcus because of the attachment of the graft to the floor of the orbit, and without this attachment the operation must be considered unsuccessful. The previously inserted interrupted sutures at the graft-conjunctiva junction are then tied together over the petrolatum gauze within. An additional petrolatum gauze pack is inserted into the socket, and the lids are sewed together with two interrupted sutures of silk. Petrolatum gauze, an eye pad and fluff gauze pressure dressing are applied.

A piece of stent, latex or sponge rubber may be used instead of the petrolatum gauze, but this is not necessary. We have sutured the graft to a latex or sponge rubber prefitted mold and inserted this mold and graft over the raw surface, but our results have not been as gratifying as with direct suture. The cheek sutures are cut the fifth day but not removed. The lid sutures are cut the seventh day. The petrolatum gauze pack is removed the ninth day, together with all the sutures, and an acrylic conformer corresponding to the shape of an artificial eye is inserted, as seen in figure 4. A certain amount of conjunctivitis will result, together with some purulent drainage. This is controlled by repeated irrigations with boric acid or some other appropriate solution. We do not wait for contraction in these cases, but the patient is fitted as soon as the socket and adjacent lid have assumed their normal appearance and all conjunctivitis and swelling have subsided.

Absence of Cul-de-Sac Due to Redundancy of Mucous Membrane.—Frequently there is absence of the cul-de-sac, and examination reveals a redundancy of conjunctiva, producing a direct continuity between the margin of the eyelid and the socket. An attempt should nevertheless be made to fit a prosthesis in a case of this type, since if the exertion of force from the upper lid or the region of the upper cul-de-sac is properly

directed and a satisfactory socket is made available it is possible that the artificial eye can be fitted and the redundant mucous membrane depressed, with the cul-de-sac assuming a normal appearance. If the artificial eye is not retained, there may be a notch available in the socket by which an appliance can be attached to the artificial eye and held by the notch. Frequently, however, regardless of what attachment is made to the artificial eye, the eye must be extremely thin and of the shell type, and it will inevitably rest on the lid rather than the sulcus or the bed prepared for it. In these circumstances, it is far more desirable to incise the conjunctiva along the inside approximately at the line of the lid-socket junction, extend the incision to the floor of the orbit, roughen or incise the periosteum, invert the edges of the conjunctiva and attach both flaps to the periosteum of the anterior portion of the rim. The same type of suture is inserted as is used in making a mucous membrane graft, only both edges of the conjunctiva are incorporated in the suture that passes through the cheek. We suggest a central point of anchorage, as well as the two lateral points. In these circumstances, a desirable sulcus will be produced. Care must be taken to leave the anterior flap of conjunctiva long enough that the lid will not be inverted and depressed after anchorage. A suture passed through the conjunctiva and anchored without incision is not sufficient. Raw edges must be produced and a new line of cleavage established.

Skin–Mucous Membrane Combination.—The combination of skin and mucous membrane as a lining for the lids and socket has been condemned by many excellent clinicians. On the other hand, it has been, and still is, used by many without any untoward effect. We see no contraindication whatever to combining the two. Battle casualties present an entirely different pathologic problem in repair. We have had cases in which we completely excised the scar tissue and inserted a mucous membrane graft, and within a few weeks the only remnant of the graft was a ball of mucous membrane incorporated in more scar tissue. Secondary repair with implantation of a thin split graft relieved the situation and gave us an excellent result. Our method of choice is always use of mucous membrane, but in extensive deformity due to scar tissue, especially in the upper cul-de-sac, and secondary contractures following mucous membrane grafts in the presence of healthy conjunctiva elsewhere within the socket or lids, we see no contraindication to use of this combination. We agree that the secretions are increased greatly for a period and desquamation exists for a time, but this condition is gradually reduced to such an extent that ordinary mechanical cleansing of the socket will relieve the situation.

Within three months to a year the graft becomes soft and flexible and is easily displaced by a prosthesis. Except for its appearance, it assumes all the characteristics of the host. In lining both lids with

skin, we still attempt to retain the central portion of the conjunctiva, provided it has a normal appearance. If the excision of the central portion is necessary, it can be done at a later stage.

Whatever procedure is employed, we cannot stress too strongly the importance of building sulci sufficiently deep, since the depth is more easily reduced by excision of the graft than increased by the addition

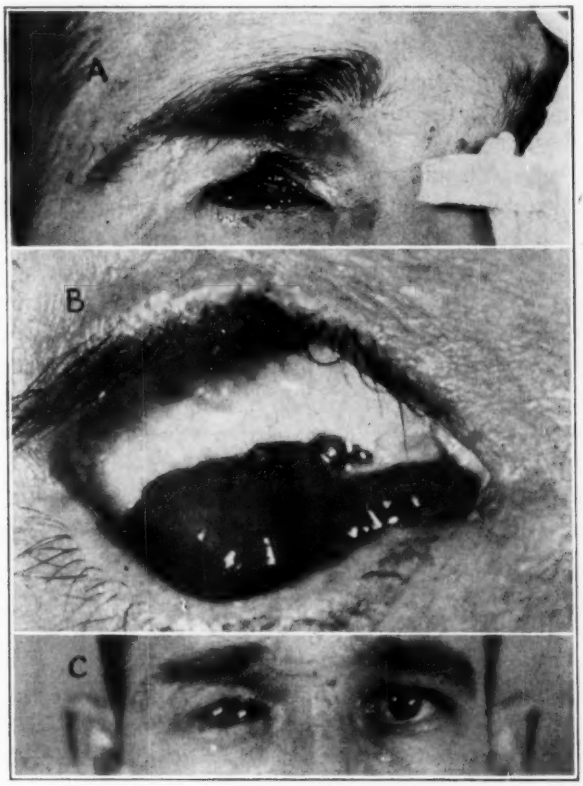

Fig. 5.—*A*, condition of the right orbital region on the patient's admission. The upper lid was adherent to the socket. Implantation of a mucous membrane graft was attempted in the superior cul-de-sac and failed. The "take" was satisfactory, but it shrank to a small area of combined mucous membrane and cicatricial tissue. Previous to this a full thickness graft from behind the ear was placed in the upper lid to lengthen the lid and release the eyebrow, which was lowered, as seen in the photograph.

B, the combined skin–mucous membrane graft in the same eye. The remnants of previously inserted mucous membrane and scar tissue were excised, and a thin split graft from the inner side of the arm was inserted. This photograph also shows the result of lengthening the upper lid with a previously applied full thickness graft. The notching was repaired by the Wheeler halving method.

C, result of the repair described in *B*. An acrylic plug was inserted and the notching corrected. The socket is ready for insertion of the artificial eye. The patient had a small bony defect beneath the outer portion of the eyebrow. A cartilage graft was contemplated, but release from assignment prevented us from carrying out the procedure.

of more graft. Full thickness mucous membrane is employed extensively. The thinner the skin graft the better, provided enough support is given to the graft over a sufficiently long period to prevent too much contracture. If skin is properly anchored, this does not become a very important factor, except in the superior cul-de-sac, where periosteal anchorage is out of the question. For this same reason, the superior cul-de-sac should be of much greater depth in order to compensate for some of its reduction in size by contracture of the graft.

Mucous membrane will not contract to the same extent, but still the graft should be wider than the raw area presenting, in order to provide for its anchorage to the orbital floor. We have lined both upper and lower cul-de-sacs with a single graft of mucous membrane but have found that the final result is not very satisfactory because of the tendency of the graft to contract in all directions toward the central portion of the socket. It is a far better procedure to line both cul-de-sacs with mucous membrane, either at the same time or at a second stage, but to interrupt the continuity of the graft at the medial and lateral canthal regions. In these cases we like to extend the graft in the inferior cul-de-sac slightly above both the inner and the outer canthal region.

Complications Existing in Socket Repair.—The caruncle is seen as inevitably attached to the socket and frequently elongated, extending in all directions. Without a visible caruncle the eye looks flat and bare at the inner canthus, and every effort should be made to reconstruct one if absent or to attempt to make it available if present. The ideal caruncle is one which is not elongated and which is just a soft, fleshy attachment of the socket, so that when the prosthesis is inserted the medial portion falls behind the caruncle in a groove which has all the appearance of having been made to receive the prosthesis. Another type is firmly attached to the socket, but there is sufficient resilience in the conjunctiva of the socket that the insertion of the prosthesis will invert the outer portion and the appearance of the medial portion will be satisfactory.

Another type of attachment in which we are chiefly interested is the caruncle that is bound down to the orbital socket with scar tissue, either attached firmly all around or in the form of a rigid band. If attached firmly, it is split, leaving a medial portion slightly larger than the normal caruncle in the good eye. The incision is then extended medially and posteriorly to the lacrimomaxillary junction. A mucous membrane graft is then inserted and attached to the periosteum, as described in repair of the inferior cul-de-sac. If attached with a scar band and in the presence of normal redundant conjunctiva, a Z plastic operation will serve the purpose, the elongated lateral portion of the caruncle being completely excised up to the required medial por-

tion. The choice of procedure should always be that which will simplify the fitting of a prosthesis and retain as normal a relationship as possible between the caruncle and the medial scleral exposure of the artificial eye.

It is important to notice the relationship of the caruncle to other structures in the normal eye. It is attached superiorly by way of the plica, and also inferiorly, but it likewise assumes an oblique position, and in many cases the apex of the triangle is attached to the lower lid, inferiorly and posteriorly.

The eye travels along the caruncle in its inferior medial portion, and an attempt should be made to place the caruncle in this position so that the artificial prosthesis can accommodate itself to as normal a position as possible.

Atony of Lower Lid as a Complication.—This condition is inevitably present in older patients and, we believe, is frequently caused by the wearing of a prosthesis over a long period. In the greater percentage of these cases no sulcus is present, or if a sulcus is present it is found near the margin of the lid rather than at the lid-socket junction. Even a shell eye worn over a long period will tend to produce an atonic condition of the lower lid, with drooping and slight ectropion. To avoid this in future fittings, we have advocated reconstruction of the inferior cul-de-sac, the degree of repair and the necessity for repair being in inverse proportion to the anteroposterior diameter of the lower lid. As the diameter, i. e., the distance from the tarsal margin of the lid to the lid-socket junction, is increased, there is less indication for surgical intervention. As the diameter decreases, up to the point where the lid and the socket are in direct continuity, the indication for operation is increased. With this procedure a new sulcus will be formed, which will permit the eye to rest within the socket rather than on the lid, and this will be a great factor in prevention of atony.

Exercises of the lower lid in cases of mild atony will frequently restore the tone of the orbicularis muscle. Employment of such exercises should be much more stressed than it is after the fitting of a satisfactory prosthesis. The patient should be placed in front of a mirror and shown how the lower lid can be raised, utilizing the musculature in the immediate vicinity, especially the orbicularis. We suggest that the patient place the finger in region of the eyebrow and produce pressure, so as not to use the frontalis and the orbicularis muscle of the upper lid in closing the eye. The principle is to raise the lower lid.

In cases of more severe atony, with dropping which borders on ectropion, seen frequently in older patients, operation should be performed even before the artificial eye is inserted. The degree of correction necessary can be determined with the first fitting of the wax plug, and the eye need not be completed until the operation has been performed. In

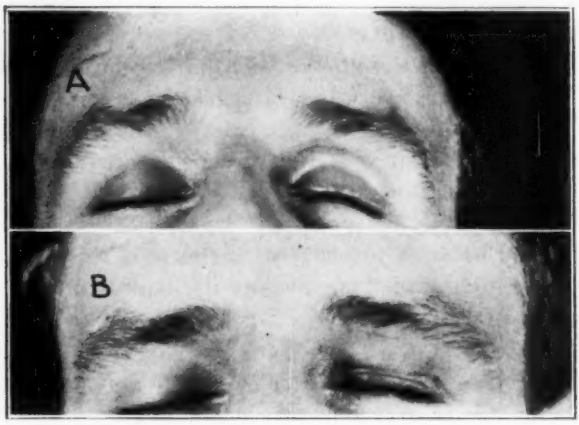

Fig. 6.—*A*, absorption of soft parts of the left orbital socket, with sunken appearance. *B*, repair with insertion of a dermal graft.

Fig. 7.—*A*, cicatricial deformity with symblepharon. Previous operations had been performed, but the patient still could not wear an artificial eye. Scar tissue extended deep into the inferior cul-de-sac. This tissue was excised, and a mucous membrane graft was inserted. *B*, result of excision of scar tissue and insertion of a mucous membrane graft. *C*, patient with the artificial eye in place.

the majority of cases of this type we prefer the Kuhnt-Szymanowski [3] procedure for the correction. The Wheeler tarsorrhaphy at the external canthus is ideal for cases of milder atony, but care should be taken with regard to the degree of closure of the palpebral fissure, so that it will not interfere with fitting of the prosthesis. There is no reason in narrowing the palpebral fissure to eliminate a prominent lateral exposure of the sclera when the narrow palpebral fissure will be the most noticeable. Again, we cannot help but stress the importance of giving the patients with mild atony at least three months' trial with exercises prior to any operative procedure. One of the complications encountered with the dropping of the lid is complete relaxation of the external canthal ligament. Repair of the canthal ligament is in order primarily because otherwise if the lower lid is shortened and the edge of the tarsal border reattached retraction of the upper lid will be produced and the upper lid will assume a semicircular appearance rather than its normal outline. Galvanocautery is not indicated in cases of this type. Complete shortening of the lower lid is the procedure of choice.

Other complications are minor defects above the orbit. Such defects are frequently important and are difficult to remedy. In the past too little stress was placed on their repair. It is not sufficient to repair the socket and neglect a notched or distorted lid or a deformity of the eyebrow. A patient will not have a good appearance, with a well fitted prosthesis and a sunken upper socket. In the present mass repair, ophthalmic surgeons are learning a good deal toward the perfecting of reparative surgery about the orbit.

A few of these minor defects are illustrated in this paper. A supplement, showing more pronounced deformities of the lids and orbit and their repair, will be presented at a later date.

CONCLUSION

In any circumstances, we feel that prior to operation the prosthetics laboratory should see the patient. With the advent of plastic eyes this is important, since the necessity for operation can be determined in a short time. There must be a closer cooperation of the prosthetics laboratory, the ophthalmologist and the plastic surgeon. True, one will not encounter cases of the type one now comes in contact with. The severity of the condition will not be as pronounced. The underlying pathologic condition will not be as great. But, as has already been mentioned, people are becoming more eye conscious, and it will tax the skill of ophthalmologists to the limit to see that they are properly fitted.

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INFLUENCE OF LOCAL ANTISEPTICS ON REGENERATION OF CORNEAL EPITHELIUM OF RABBITS

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DURING World War II the incidence of ocular injuries was unusually high. Recent reports have pointed out that a wide variety of agents affect adversely the healing of the epithelial defects of the cornea. No agent has yet been discovered which increases the rate of healing.

I [1] have demonstrated that sulfonamide compounds in the form of powder, ointment or emulsion retard the regeneration of the epithelium of the cornea and promote the formation of scar tissue and vascularization. Smelser and Ozanics [2] showed that sulfathiazole and sulfacetimide inhibit cell migration after corneal burns. Sulfadiazine and penicillin produce only slight inhibitory effects. Berens, de Gara and Loutfallah [3] demonstrated that corneal wounds healed more slowly when treated with a sulfonamide ointment or with the ointment base alone than when the wounds were untreated. Sulfonamide ointment delayed the healing of deeper wounds more than that of superficial ones. Leopold and Steele [4] found that the retarding effect of sulfonamide drugs was greater in corneas in which the denudation involved the limbus than in those in which the limbus was not involved. They stated that the differences in retarding or scarring effects between ointment bases or powder bases alone and those containing sulfonamide compounds were insignificant.

From the Department of Ophthalmology, Northwestern University Medical School.

Dr. K. K. Chen and his associates, of the Lilly Research Laboratories, gave valuable aid in this work.

1. Bellows, J. G., and Gluckman, R.: Local Toxic Effects of Sulfanilamide and Some of Its Derivatives, Arch. Ophth. **30**:65 (July) 1943.

2. Smelser, G. K., and Ozanics, V.: Effect of Chemotherapeutic Agents on Cell Division and Healing of Corneal Burns and Abrasions in Rat, Am. J. Ophth. **27**:1063, 1944.

3. Berens, C.; De Gara, P. F., and Loutfallah, M.: Effect of Sulfonamide Ointment on Healing of Experimental Wounds of Rabbit Cornea, Arch. Ophth. **30**:631 (Nov.) 1943.

4. Leopold, I. H., and Steele, W. H.: Influence of Local Application of Sulfonamide Compounds and Their Vehicles on Regeneration of Corneal Epithelium, Arch. Ophth. **33**:463 (June) 1945.

Gundersen and Liebman [5] determined experimentally the effect of local anesthetics on the regeneration of corneal epithelium. The sulfate of butacaine and the hydrochlorides of cocaine, tetracaine, phenacaine and larocaine were found to delay the healing process of the corneal epithelium of the guinea pig. It was demonstrated that the concentration and toxicity of the preparation modify the effects. Smelser [6] reported that the common local anesthetics retard the migration of epithelial cells over the burned area.

Friedenwald and his co-workers [7] studied the mitotic and wound-healing activities of the corneal epithelium. They found that histamine, acetylcholine, physostigmine, carbaminoylcholine chloride and atropine are without effect on the mitotic activity. Epinephrine and ephedrine suppress mitosis. After the removal of the superior cervical sympathetic ganglion, colchicine causes a sharp drop in the rate at which cells enter mitosis. Mechanical damage, ultraviolet and beta radiation, cold, vitamin A deficiency and local and general anesthetics, such as cocaine, ether and barbiturates, inhibit mitosis.

In view of the fact that most surgeons in treating a corneal wound employ an antiseptic to decrease the possibility of infection, and since up to the present time there has been no report showing the effects of antibacterial agents commonly used in ocular therapeutics on the regeneration of the corneal epithelium, the following report is presented.

METHOD

Young adult rabbits, weighing approximately 2 Kg., were employed in this investigation. The cornea was anesthetized with a 4 per cent solution of cocaine hydrochloride, chosen not only for its anesthetic qualities but for its drying effect, which facilitated the removal of the epithelium; this was accomplished by rubbing the cornea with dry gauze; to make certain that the entire cornea was denuded of its epithelium, the eyes were stained with fluorescein. The

5. Gundersen, T., and Liebman, S. D.: Effect of Local Anesthetics on Regeneration of Corneal Epithelium, Arch. Ophth. **31**:29 (Jan.) 1944.

6. Smelser, G. K.: Effect of Local Anesthetics on Healing of Burns of the Cornea, Arch. Ophth. **33**:254 (March) 1945.

7. Buschke, W.; Friedenwald, J. S., and Fleischmann, W.: Studies on the Mitotic Activity of the Corneal Epithelium: Methods; the Effects of Colchicine, Ether, Cocaine, and Ephedrin, Bull. Johns Hopkins Hosp. **73**:143, 1943. Friedenwald, J. S., and Buschke, W.: The Influence of Some Experimental Variables on the Epithelial Movements in the Healing of Corneal Wounds, J. Cell. & Comp. Physiol. **23**:95, 1944; The Effects of Excitement, of Epinephrine and of Sympathectomy on the Mitotic Activity of the Corneal Epithelium in Rats, Am. J. Physiol. **141**:689, 1944; Mitotic and Wound-Healing Activities of the Corneal Epithelium, Arch. Ophth. **32**:410 (Nov.) 1944.

course of regeneration was observed by daily examination, facilitated by fluorescein staining.

The agents employed in this investigation were instilled in the left eyes of rabbits three times daily, while the right, or control, eye received a similar amount of isotonic solution of sodium chloride. Five rabbits was the minimum number used for each drug. Aqueous solutions of the following substances were investi-

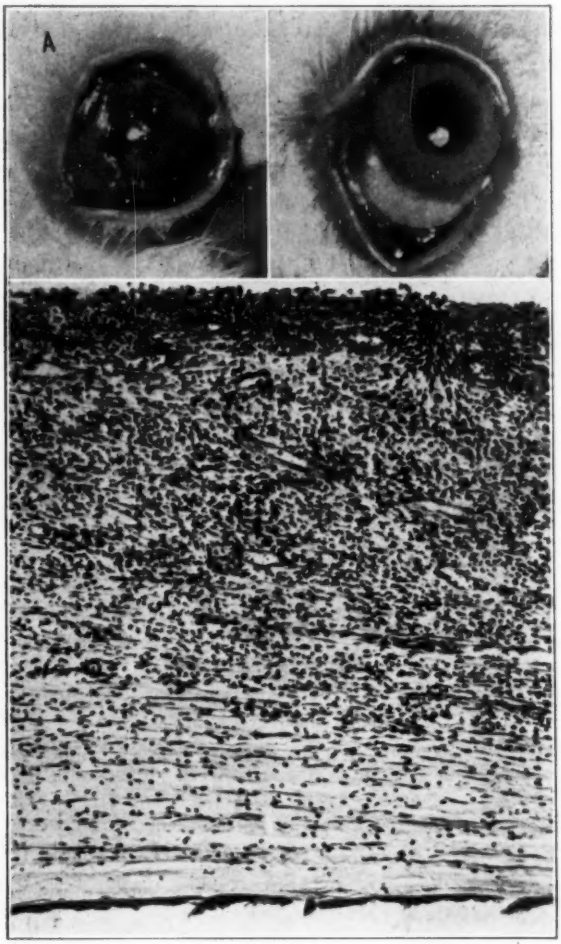

Fig. 1.—*A*, effect of 10 per cent mild silver protein on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with mild silver protein (× 111).

gated: mild silver protein (10 per cent), zinc sulfate (0.5 per cent), merbromin (2 per cent), phemerol chloride (1:2,500 concentration in 2 per cent boric acid solution), mercuric oxycyanide (1:5,000), metaphen (1:2,500), merthiolate (1:2,500), acriflavine (1:1,000), zephiran chloride (1:3,000), penicillin (1 cc. containing 2,500 Oxford units) and sodium sulfathiazole (2 per cent).

RESULTS

During the first twenty-four hours the treated and untreated eyes were clinically indistinguishable. There were haziness of the cornea and generalized congestion of the conjunctiva. After this period the return of the corneal luster in the periphery of the cornea and the failure of

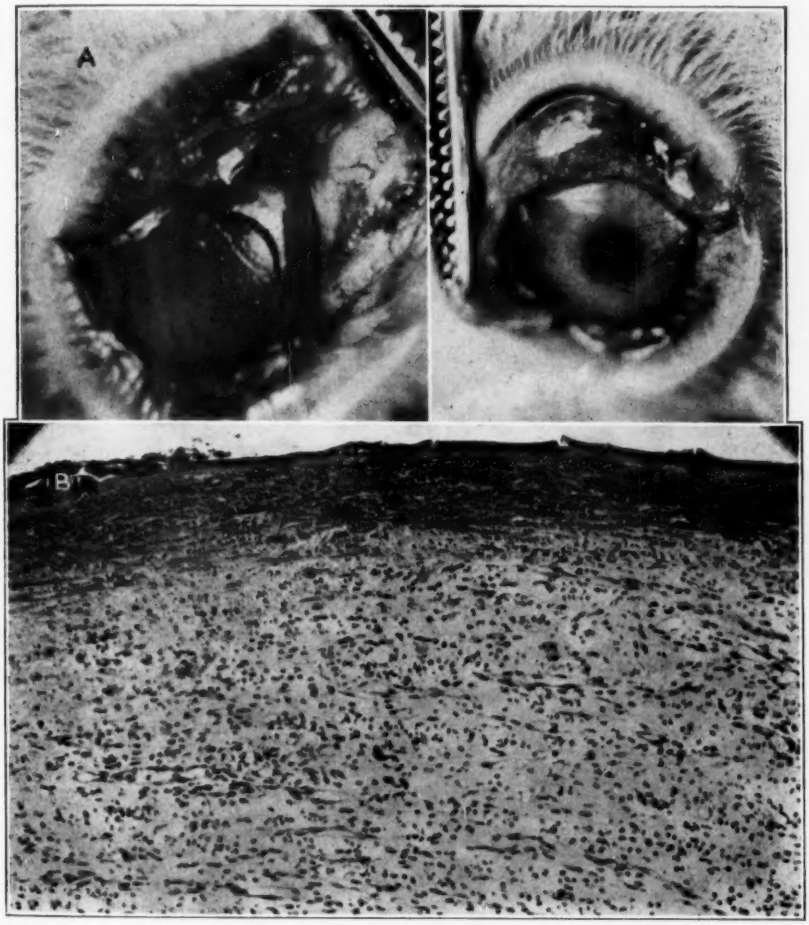

Fig. 2.—*A*, effect of 2 per cent merbromin on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with merbromin (× 111).

the corresponding area to stain with fluorescein indicated the return of the epithelial covering in that region. Nearly all the untreated eyes appeared clinically normal in four to six days, while the eyes treated with the common local antiseptics still showed large denuded areas (table).

Mild Silver Protein, 10 Per Cent.—The corneas treated with mild silver protein, even fifteen days after the denudation, had central dark-staining areas, which remained permanently opaque. Vascularization was pronounced (fig. 1 *A*). Histologic examination of the corneas removed after fifteen days showed that those of the control eyes were

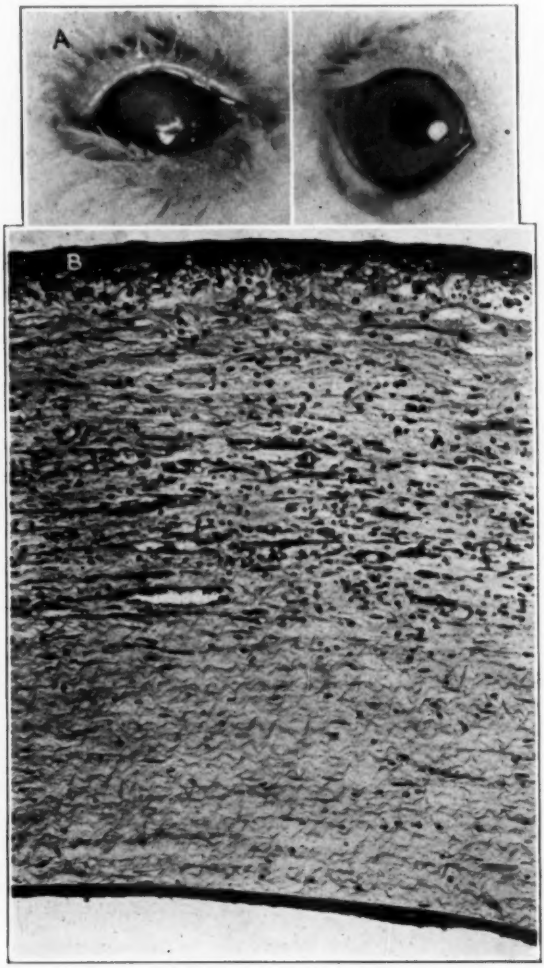

Fig. 3.—*A*, effect of 0.5 per cent zinc sulfate on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with zinc sulfate (× 111).

normal. The corneas treated with mild silver protein were thickened by marked leukocytic infiltration and moderate edema. Vascularization was prominent. The epithelium was entirely absent, and the base of the

ulceration consisted of a dense layer of leukocytes, a few fibroblasts and remnants of corneal tissue (fig. 1 *B*).

Merbromin, 2 Per Cent Solution.—A 2 per cent solution of merbromin greatly retarded the regeneration of the corneal epithelium and finally produced a dense, deep red opacity involving the entire cornea (fig. 2 *A*). Microscopic examination revealed a cornea thickened by edema, leukocytic infiltration and vascularization (fig. 2 *B*).

Zinc Sulfate, 0.5 Per Cent Solution.—Zinc sulfate in 0.5 per cent solution applied three times daily to the denuded corneas delayed the regeneration of the epithelium. A dense white opacity involving the

Time Required for Regeneration of Corneal Epithelium

Drug	Concentration	Number of Days		Condition of Cornea
		Treated Eye	Control Eye	
Mild protein silver	10%	15+	6	Opacity present
Merbromin	2%	15+	4	Opacity present
Zinc sulfate	0.5%	13	4	Opacity present
Zephiran chloride	1:3,000	15+	4	Opacity present
Acriflavine	1:1,000	15+	5	Opacity present
Metaphen	1:2,500	13	5	Opacity present
Merthiolate	1:2,500	13	6	Opacity present
Mercuric oxycyanide	1:5,000	11	5	Opacity present
Sulfonamide compounds * (Powder, Emulsion, Ointment)	.....	13+	5	Opacity present
Phemerol chloride	1:5,000	7	5	Clear
Penicillin	1 cc. = 2,500 Oxford units	4	4	Clear
Sodium sulfathiazole	2%	5	4	Clear

* Data from Bellows.[1]

entire cornea resulted from the use of this drug (fig. 3 *A*). Microscopic examination disclosed edema, leukocytic infiltration and vascularization of the cornea (fig. 3 *B*).

Zephiran Chloride, 1:3,000 Aqueous Solution.—Zephiran chloride in 1:3,000 concentration caused a delay in healing similar to that produced by the aforementioned drugs. At the end of fifteen days there was a dense central scar. Vascularization was conspicuous at the periphery (fig. 4 *A*). Microscopic examination of the cornea removed on the fifteenth day revealed pronounced edema with moderate vascularization and leukocytic infiltration (fig. 4 *B*).

Acriflavine, 1:1,000 Aqueous Solution.—Acriflavine in 1:1,000 concentration delayed epithelization and caused a dense scar to form in the cornea (fig. 5 *A*). The cornea removed on the fifteenth day revealed

microscopically variations in thickness of the epithelium. Beneath the epithelium were fibroblastic proliferation and cystic spaces, while deeper in the cornea there were edema, vascularization and leukocytic infiltrations (fig. 5 *B*).

Metaphen, 1:2,500 Aqueous Solution.—Metaphen in 1:2,500 concentration retarded epithelization and produced scar formation of the

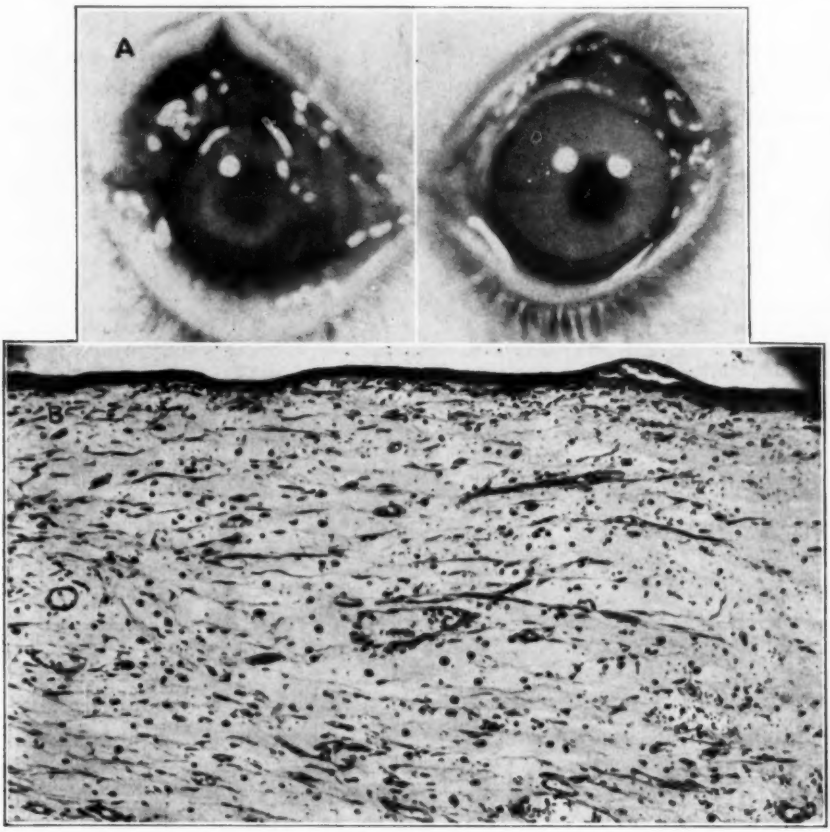

Fig. 4.—*A*, effect of zephiran chloride in 1:3,000 aqueous solution on denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with zephiran chloride (× 111).

cornea (fig. 6 *A*). Histologic examination of the cornea removed on the fifteenth day revealed an edematous, infiltrated and vascularized cornea with fibroblastic proliferation (fig. 6 *B*).

Merthiolate, 1:2,500 Aqueous Solution.—Merthiolate in 1:2,500 concentration also delayed the epithelization of the cornea, producing scarring with vascularization (fig. 7 *A*). Microscopic examination of

an eye removed on the fifteenth day showed intense corneal edema with a moderate degree of vascularization and leukocytic infiltration (fig. 7 *B*).

Mercuric Oxycyanide, 1:5,000 Aqueous Solution.—Mercuric oxycyanide in 1:5,000 aqueous solution caused a delay in epithelization of the denuded cornea and produced a permanent scar on the cornea (fig. 8 *A*). Histologic examination revealed that the cornea was thick-

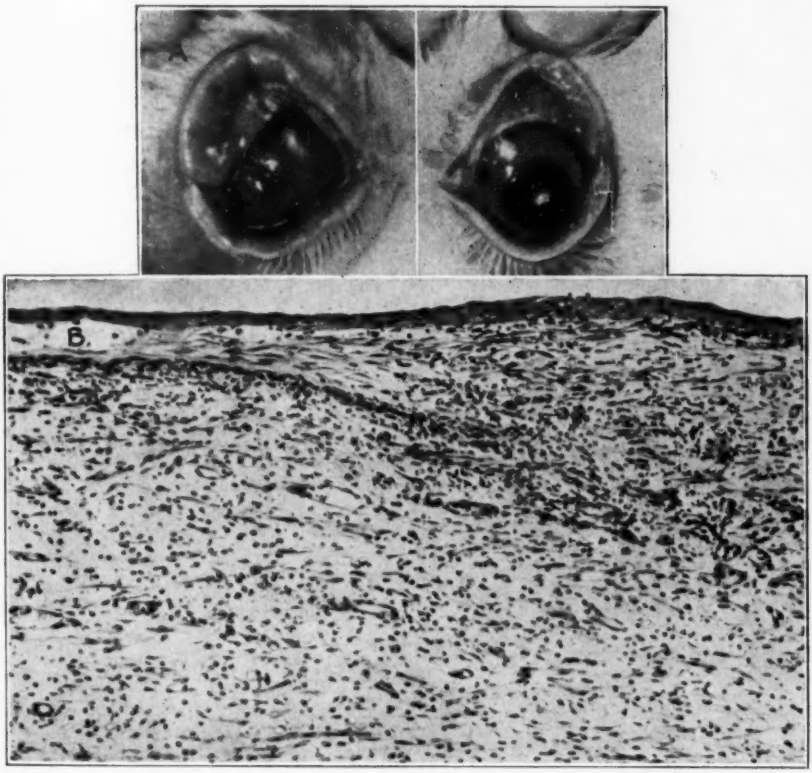

Fig. 5.—*A*, effect of acrifavine in 1:1,000 solution on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of the cornea treated with acriflavine (× 111).

ened by edema, leukocytic infiltration and vascularization. Fibroblastic proliferation was found beneath the epithelium (fig. 8 *B*).

Sulfonamide Compounds.—In a previous report [1] it was shown that sulfanilamide, sulfathiazole, sulfadiazine and sulfapyridine applied to the denuded cornea in the form of a powder, ointment or emulsion delayed the reformation of the epithelial layer and caused a scar to form on the

cornea. In the present investigation, a 2 per cent solution of sodium sulfathiazole caused neither delay in epithelization nor scarring of the cornea.

Phemerol Chloride, 1:5000 Aqueous Solution.—Phemerol chloride in 1:5,000 concentration in 2 per cent boric acid solution delayed

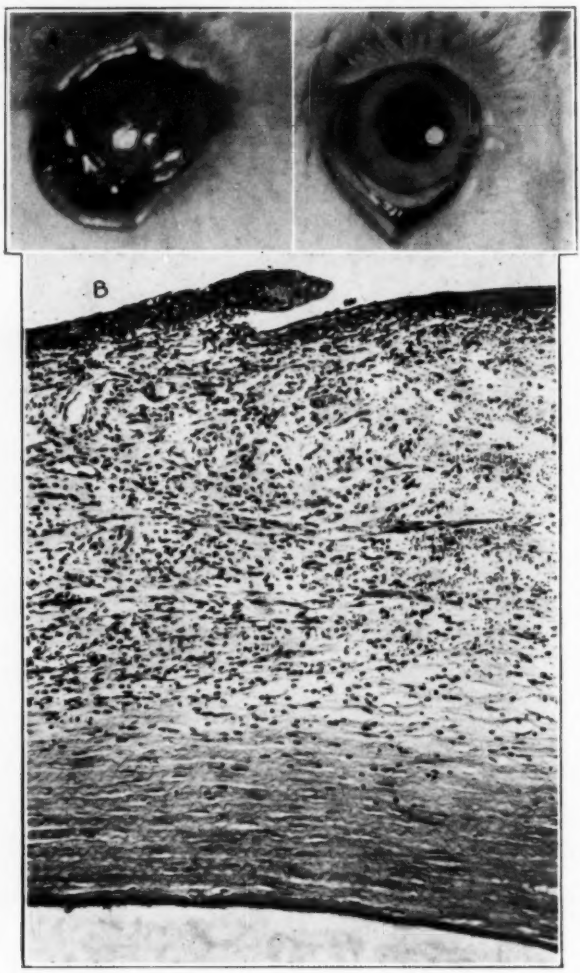

Fig. 6.—*A*, effect of a 1:2,500 aqueous solution of metaphen on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with metaphen (× 111).

epithelization by only a few days. No permanent opacity formed on the cornea, and histologic examination disclosed an unaltered cornea (fig. 9).

Penicillin (1 cc. containing 2,500 Oxford units).—Penicillin neither delayed the regrowth of the epithelium of the cornea nor caused scar formation. Microscopic examination disclosed no changes in the cornea (fig. 10).

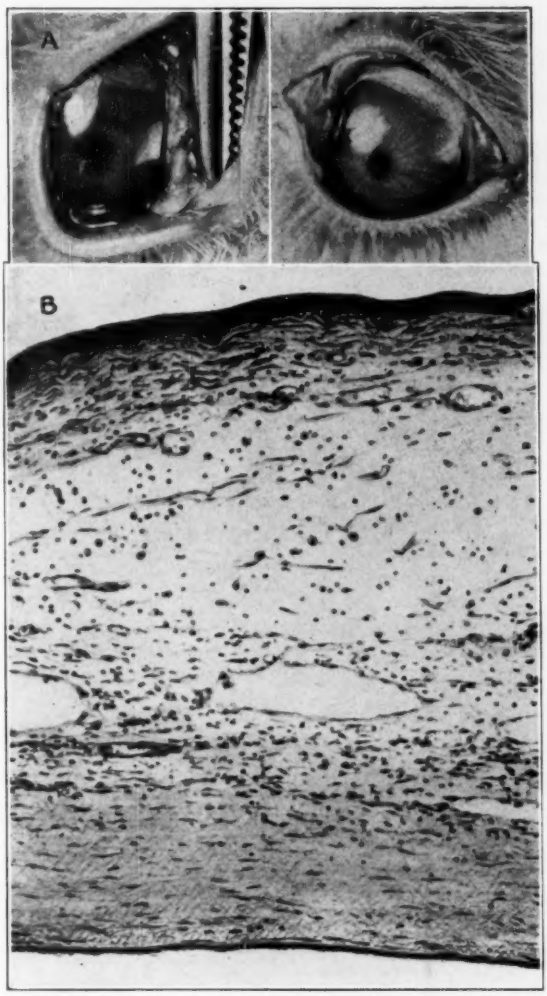

Fig. 7.—*A*, effect of a 1:2,500 per cent aqueous solution of merthiolate on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with merthiolate (× 111).

SUMMARY AND CONCLUSIONS

The results of this investigation disclosed that the local antiseptics ordinarily employed in ocular therapeutics (mild silver protein, merbromin, zinc sulfate, zephiran chloride, acriflavine, metaphen, merthio-

late and mercuric oxycyanide) had considerable delaying effect on the healing process of the corneal epithelium of rabbits. In most instances these drugs caused a permanent opacity of the cornea. Microscopic examination of the corneas showed edema, leukocytic infiltration, fibroblastic proliferation and vascularization. Since the same histologic

Fig. 8.—*A*, effect of mercuric oxycyanide in 1:5,000 aqueous solution on the denuded cornea (left) of treated eye and (right) of control eye. *B*, section of cornea treated with mercuric oxycyanide (× 111).

changes were produced by various therapeutic agents differing greatly in chemical constitution, it would appear that the corneal changes were due to a nonspecific irritation rather than to a specific chemical effect.

Phemerol chloride in 1 : 5,000 concentration in 2 per cent boric acid solution delayed the healing only slightly and produced no permanent alterations in the cornea. Sodium sulfathiazole, in 2 per cent aqueous solution, and penicillin, in a concentration in which 1 cc. contained 2,500 Oxford units, neither delayed the regeneration of the epithelial covering nor produced corneal opacities.

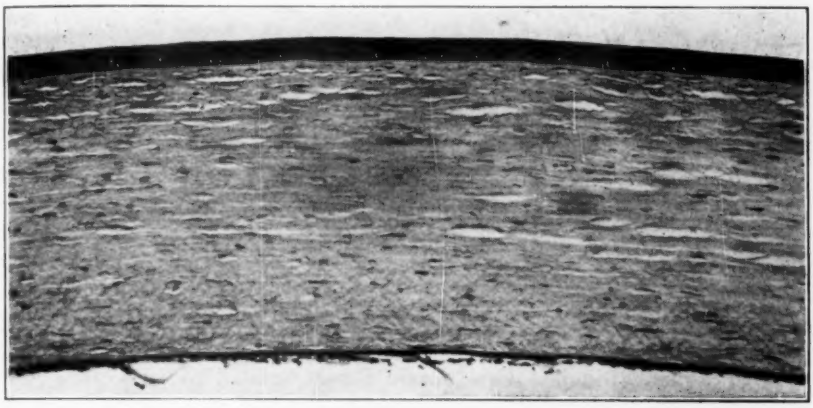

Fig. 9.—Section of cornea treated with phemerol chloride 1 : 5,000 concentration in 2 per cent boric acid solution (× 111).

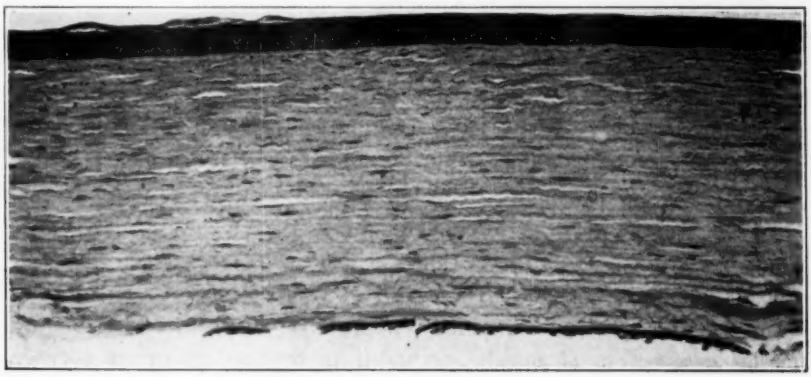

Fig. 10.—Section of cornea treated with penicillin (1 cc. containing 2,500 Oxford units) (× 111).

In conclusion, repeated instillations of the common local antiseptics are not recommended in the treatment of corneal injuries. When the possibility of infection is great, the aqueous solution of sodium sulfathiazole or penicillin may be used.

HEREDITARY DISK-SHAPED (RING) CATARACT

Report on a Family, with Microscopic Examination of an Eye

ENRIQUE SAMUEL HARO, M.D.
LIMA, PERU

THE DISK-SHAPED, or ring, cataract is a rare form of congenital cataract that has been reported relatively few times. Judging from a review of the literature, the hereditary tendency has been reported in only 1 family. In July 1944 a 10 year old girl (Nadine L.) with congenital disk-shaped cataracts was brought to the eye clinic of Stanford University Hospital for examination and treatment. Her history led to the study of a most interesting family, consisting of 59 persons, of whom 16 have the same congenital anomaly.

In addition to the cataract, all the affected members examined showed symmetric dislocation of the lens. No other local or systemic anomalies were found. This family is not related to any other with congenital cataract, and, so far as I can trace the familial history, there were no known cases of this condition prior to the ones reported herein. There was no history of consanguinity.

One of the eyes examined was enucleated after a traumatic laceration and was studied microscopically.

The study of congenital hereditary cataract has shown that there is a tendency to uniformity in the type within any family line. However, while this is usually true, Lutman and Neel [1] pointed out that it is sometimes found that certain of the cataractous persons in a given pedigree have a type of opacity of the lens that differs materially from the type present in other affected members of the family. Of interest in any hereditary condition is the exact nature of the defect; its origin, when suddenly appearing in a healthy strain of persons; the mode of transmission, and the variability within the group. However, congenital cataract must not be regarded merely as an opaque lens; it is "a part of the whole cycle of events." [2] Often other abnormalities are present. All this involves an important sociologic problem, especially

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Dr. Haro made this study while holding the Kellogg Foundation Scholarship in the Department of Ophthalmology, Stanford University School of Medicine, San Francisco.

1. Lutman, F. C., and Neel, J. V.: Inherited Cataract in the B Genealogy, Arch. Ophth. **33**:341 (May) 1945.

2. Fox, L. W.: Congenital Cataract, J. A. M. A. **89**:2249 (Dec. 31) 1927.

if it is true, as Nettleship [3] and others have stated, that persons with hereditary imperfections and disease are as a rule members of unusually large pedigrees.

CLINICAL APPEARANCE OF DISK-SHAPED CATARACT

The disk-shaped cataract is characterized by the presence of a central opacity at a distinctly deeper level than the remainder of the surface of the lens, with some irregular opacities in the immediate vicinity of the central patch, in which the latter appears to be engraved. With a small pupil the central opacity may fill the entire pupillary area; if sufficient dilation is obtained, a peripheral clear zone can be seen.

The lens in some instances appears smaller than usual. It is thin anteroposteriorly, especially in the center, owing to the absence of the central structures. This hollowed portion is closed by a membrane

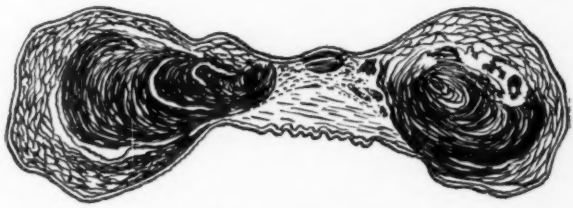

Fig. 1.—Sagittal section of a disk-shaped, or "ring" cataract. The lens appears as a dumbbell, having two lateral masses connected by a central band.

more or less thick and opaque, similar to a secondary cataract. This laminated mass of tissue, according to pathologic studies (fig. 5), consists of three layers: the anterior and the posterior lens capsule, with the remains of the epithelium of the lens, showing a variable amount of proliferation, between them. There is no intermediate lens substance proper in this portion. In all the rest of the lens cortex is present, but with some disturbance around the central defect. This defect forms an opaque ring, becoming clearer toward the periphery. The opacity within the ring itself has in most cases a similarity to lamellar cataract, with several concentric zones.

The central defect varies in size and corresponds roughly to the diameter of the embryonic nucleus.

The lens as a whole has the shape of a ring, like a life belt. In sections it appears as a dumbbell, having two lateral masses connected by a central band (fig. 1).

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3. Nettleship, E.: On Some Hereditary Diseases of the Eye, Tr. Ophth. Soc. U. Kingdom **29**:57, 1909.

PEDIGREE OF THE L. FAMILY

Compiling the family data of the reported cases was rather difficult, inasmuch as many members live in other states. The few in San Jose, Calif., willingly gave information as accurately as possible. They did not know personally several members of the family; moreover, the oldest one alive was the ninth child of his sibship, and some of his brothers and sisters died before he was born or when he was too young to remember any relevant facts about them. However, the information obtained after several rechecks with various relatives, with elimination of the doubtful facts, can be considered dependable. The family contacts have been fairly close. All the informants were deeply concerned about the condition present in such a high percentage in the family and remembered rather accurately the facts related to it.

About the middle of the last century the first members of the family of whom anything is known came to the United States and settled in Springfield, Mo. A detailed description of the genealogy follows.

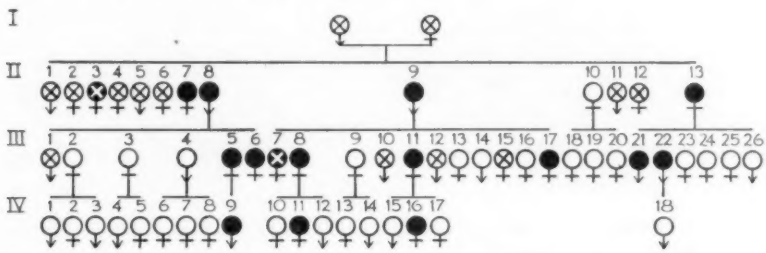

Fig. 2.—Family tree. Affected members are indicated by black circles; members who have died, by circles with crosses, and affected members who have died, by black circles with white crosses.

I 1[4]: Mr. France L. came from Ireland. He was a healthy man and had good vision. Late in his life he wore glasses "just for reading." He died at the age of 74 of some type of renal disease.

I 2: Mrs. Sara L. came from England. She was known to have good vision and to be healthy. She also wore glasses for reading only late in her life. She died of a "stroke" at the age of 72.

This marriage had an issue of 13 children.

II 1: Virgil L. was not affected. He died at the age of 3 months of diphtheria.

II 2: Clara L. was not affected. She died at the age of 7 months of pneumonia.

II 3: Beckey L. had congenital cataracts. She died at the age of 19 of typhoid.

II 4: Carmen L. was not affected. She died at the age of 22 as a result of an accident.

4. The Roman numeral indicates the generation; the arabic numeral, the individual number in the family generation (fig. 2).

II 5: Oscar L. was not affected. He died at the age of 17 as a result of an accident.

II 6: X. L. was a stillborn girl.

II 7: Myrthle L. was 62 years old; she had congenital cataracts. She had been seen by ophthalmologists but had never had an operation. Her vision was very poor; she could see only large objects and was unable to read. She was a widow and had no children.

II 8: William L. was 60 years old. He had congenital cataracts but had had no operation. He could see just "enough to get around" but could not read. He was married and had 6 children.

III 1: Otis L. was not affected. He died at the age of 10 years of whooping cough.

III 2: Opal P., aged 34, was not affected. She was married and had 3 children.

IV 1: Pat P., aged 13, was not affected.

IV 2: Dorothy P., aged 10, was not affected.

IV 3: James P., aged 8, was not affected.

III 3: Leora S., aged 31, was not affected. She was married and had 2 children.

IV 4: Edward S., aged 14, was not affected.

IV 5: Joan S., aged 10 was not affected.

III 4: Lye L., aged 29, was not affected. He was married and had 3 children.

IV 6: Evelyn L., aged 8, was not affected.

IV 7: Lucell L., aged 6, was not affected.

IV 8: Loretta L., aged 4, was not affected.

III 5: Helen L., aged 21, had congenital cataracts and was operated on three times ("needlings"). Good vision was obtained, which allowed her to go through school successfully. She was married and had 1 child.

IV 9: Joe L., aged 3, had congenital cataracts; vision seemed to be very poor. He had had no medical attention at the time of the study.

III 6: Wally L., aged 14, had congenital cataracts. Four needling operations were performed, with resulting fairly good vision. She was going to school.

All the persons so far spoken of, descendants of William L. (II 8), live at Springfield, Mo.

II 9: Grover L.,[5] aged 56, was the next member of the second generation. When he was a few months old, his eyes were examined, and the diagnosis of congenital cataracts was made. He was seen by several ophthalmologists, but no operation was attempted; he did not know why. He had noticed no decided change in vision; he also stated that he could see better at night. General examination showed a tall, apparently strong and healthy man.

Ophthalmologic Examination.—The patient had an esotropia of about 15 degrees, fixing with the left eye most of the time. External examination revealed nothing abnormal.

5. This patient was examined in the present study.

Vision with a small pupil was limited to perception of hand movements at 5 feet (1.5 meters) in the right eye and to counting fingers at 5 feet in the left eye. He could not read at all with the right eye. He read Jaeger type 20, poorly, with the left eye, holding the card very close. The pupils were dilated with eucatropine hydrochloride, 3 per cent; under this condition vision was limited to perception of hand movements at 5 feet and to counting fingers at 10 feet (3 meters) in the left eye. Manifest refraction showed no improvement in the right eye, but vision in the left eye with a + 11.00 D. sphere, improved to 15/200; with a + 3.00 D. sphere addition, he read Jaeger type 10 to 12.

Examination with the slit lamp revealed interesting features (fig. 3).

Right Eye: The anterior chamber was deep; there was pronounced iridodonesis, and the lens was dislocated nasally and upward, leaving a rim temporally and inferiorly through which the zonular fibers could be seen. The whole lens was opaque and seemed somewhat smaller than usual; it could be described as

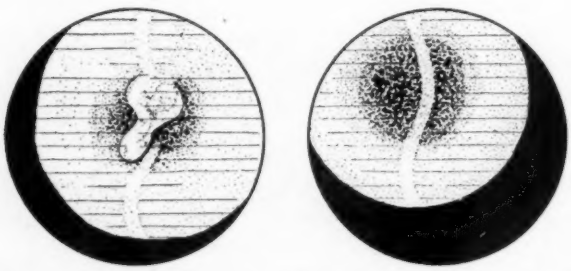

Fig. 3.—Eyes of Grover L. (II 9). The sketch represents the appearance of the lenses as seen with the slit lamp. Both lenses are white, doughnut-shaped and greatly dislocated, especially the left. The central hollow of the right lens is filled with white, loose material.

a "white doughnut," with the center partially filled with loose, flocculent material, such as is seen after a discission, placed behind the capsule and at a deeper level than the periphery of the lens. The central pitlike portion could barely be seen because of the loose material which filled it.

Left Eye: The chamber was also deep, with pronounced iridodonesis. The lens was small and extremely dislocated nasally and upward, so that the equator formed a broad crescent, with the edge of the dilated pupil in the inferior third, through which the fundus could easily be seen. The whole lens was opaque, and the name "white doughnut" was more appropriate for the lens on this side than for that on the other, as the central portion was very thin, almost clear, with just a fine membrane partially hidden behind the pupillary border superiorly (fig. 3). The zonular fibers were present only at the edges of the crescent.

Fundi: The fundus was not well seen in the right eye; no abnormalities were noted in the left.

Descendants.—He was married and had 11 children.

III 7: Lucille L. had congenital cataracts and died at the age of 9 of typhoid.

III 8: Maudie D.,[5] aged 30, had congenital cataracts. She was operated on four times when she was 17 years of age. It was stated that such operations were "needlings," but clear and sharp cuts at either side of the fairly dense membrane in each eye suggested another type of intervention.

Vision was 20/200 in the right eye (with +11.00 D. sph. ⊃ +1.50 D. cyl. axis 90) and 20/30 in the left eye (with + 11.50 D. sph.).

The patient read Jaeger type 12 with the right eye and Jaeger type 4 with the left eye (with a + 3.00 D. sphere addition).

External examination revealed nothing abnormal. The pupils were clear; after dilation, rests of fairly dense membranes could be seen, as already stated.

The fundi showed no abnormalities.

She was married and had 3 children.

IV 10: Dolores D.,[5] aged 8 was not affected.

IV 11: Doris D.,[5] a clinic patient, was 5 years old at the time of the study. The parents noticed cataract in both eyes at the age of 2½ months. Vision seemed not to have changed up to the time of this examination.

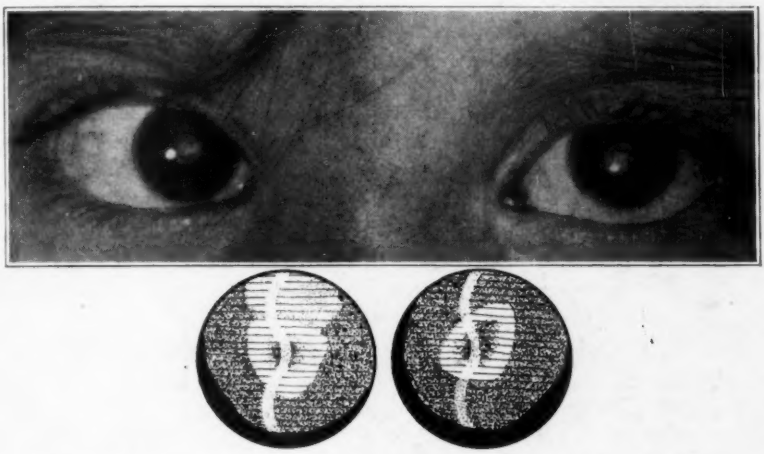

Fig. 4.—Eyes of Doris D. (IV 11). Note the clear periphery and the opaque, hollowed center in each lens. The right eye was enucleated after an injury, so that a pathologic study was possible. See the pathologic report and the photomicrographs (fig. 5).

Ophthalmologic Study.—On the child's entry, vision was limited to perception of hand movements at 1 foot (30 cm.) in the right eye and of hand movements at 6 feet (1.8 meters) in the left eye. (It was not improved after dilation of the pupil.) External examination revealed nothing abnormal except for bilateral "searching" nystagmus. Examination with the slit lamp showed an interesting condition.

Right Eye: With a dilated pupil, the lens as a whole appeared like a "doughnut," with the three parts characteristic of this type of cataract: the clear periphery; the central opaque membrane, at a deeper level than the periphery, and an intermediate zone, also opaque, with clear cortex anteriorly. The last structure was placed superiorly and extended from the edge of the hollowed center to the equator (fig. 4). The lens was dislocated nasally and upward, leaving a well defined rim temporally and inferiorly, through which the zonular fibers could be seen, except for a small portion where the edge of the lens was somewhat flattened.

Left Eye: With dilated pupil, the appearance of the lens was similar to that of the lens in the right eye. The dislocation was symmetric; there was also a flattened portion. In this lens there were only two parts: the white, opaque and hollowed central area, well outlined; and a clear periphery (fig. 4).

The fundi showed no abnormalities.

Operation.—Three discissions were performed on the left eye, but they were only partially successful, as the tough central opaque portion could hardly be cut. The small openings made were closed almost completely. In the fourth operation, de Wecker's scissors were inserted through a keratome incision and the membrane was cut, obtaining a large pupillary opening. Vision improved to 20/200 (with a correction of + 11.00 D. sph.). Unfortunately, the right eye had to be enucleated after a traumatic laceration near the ciliary body with extensive loss of vitreous. Examination of the specimen confirmed the clinical diagnosis as to the type of cataract, as will be seen from the pathologic report and the photomicrographs (fig. 5).

IV 12: Charles D.,[5] aged 4 years, was not affected.

III 9: Mildred B., aged 28, was not affected. She was married, and had 2 children.

IV 13: Ettarey B.,[5] aged 10, was not affected.

IV 14: Ronald B.,[5] aged 3, was not affected. Ophthalmologic examination showed remains of the pupillary membrane (from 7 o'clock to the center of the pupil in the left eye).

III 10: X. L., a boy, died a few hours after birth.

III 11: Vera T.,[5] aged 25, a clinic patient, had congenital cataracts and was operated on when 15 years old. Four needlings were performed, and fairly good vision resulted.

Ophthalmologic Study.—Right Eye: 15/100 (with + 12.00 D. sph.). Left Eye: 15/70 (with + 12.00 D. sph.). She read Jaeger type 12 with the right eye and Jaeger type 10 (with + 3.00 D. sph. addition) with the left eye. External examination showed exotropia of about 15 degrees. Examination with the slit lamp showed a deep anterior chamber in both eyes. With dilated pupils, a moderately opaque membrane with a clear large opening in both pupillary areas could be seen. The fundi were normal.

Descendants.—She is married and has 3 children.

IV 15: Billy T.,[5] aged 5, was not affected.

IV 16: Mary T.,[5] aged 4, a clinic patient, was 2 months old when the presence of cataracts was noted. Vision seemed to be fair, and better in the left eye, although no accurate test was possible. External examination revealed nothing significant except for a pronounced exotropia, the patient fixing with the left eye.

Ophthalmologic Examination.—Examination with the slit lamp after dilation of the pupils revealed the following condition:

Right Eye: There was moderate dislocation of the lens, nasally and upward, leaving a narrow rim below. The zonular fibers were intact. The lens itself had three parts: a central opaque, somewhat hollowed area; an intermediate zone, less opaque, with clear cortex anteriorly, extending mostly to the temporal side, above, and a clear periphery (fig. 6).

Left Eye: There was a symmetric dislocation of the lens, which consisted of two well defined parts: the clear periphery and a central white ring with a very deep and clear center. This ring was about one-third the total diameter (fig. 6).

Fig. 5.—*A*, anterior part of the eye enucleated from Doris D. (IV 11), showing the "annular" cataract. *B*, microscopic appearance of the lens at the edge of the central "patch" (see pathologic report).

The fundi were normal. This patient had had no surgical treatment as yet.

IV 17: Marge T.,[5] aged 1 year, was not affected.

III 12: Frances L. was not affected. She died at the age of 11 years of diphtheria.

III 13: Guleen F., aged 20, was not affected. She was married and had no children.

III 14: Roy L.,[5] aged 17, was not affected.

III 15: X. L., a girl, was stillborn.

III 16: Irene L.,[5] aged 14, was not affected. Examination revealed a strand, remnant of the pupillary membrane, running from 8 o'clock to the center of the lens in the left eye.

III 17: Nadine L.,[5] aged 10, was a clinic patient. At the age of 2 months cataracts were discovered in both eyes. They seemed not to have changed since that time. Vision also had not changed. On her admission visual acuity was 4/200 in the right eye and 20/200 in the left eye.

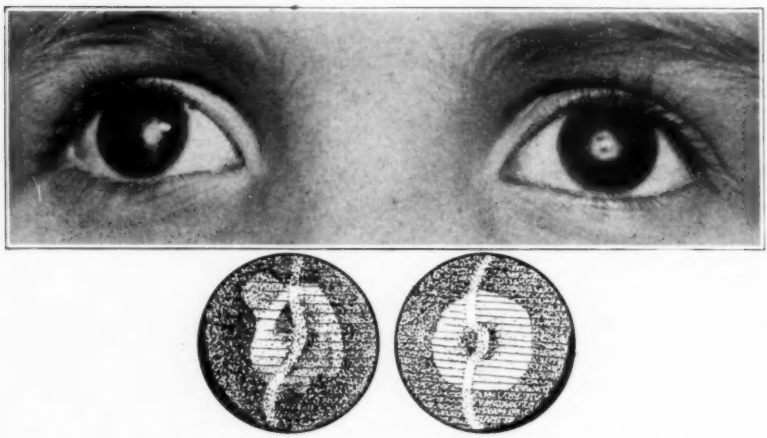

Fig. 6.—Eyes of Mary T. (IV 16). Both lenses are slightly dislocated. The right one represents a moderately hollowed, opaque central patch with some surrounding irregular opacities and a clear periphery. The left lens has a central ring with a deep clear center. The periphery is also clear.

This girl had been to school and had learned some letters of the alphabet but was unable to read.

External examination revealed nothing of significance.

Examination with Slit Lamp.—Right Eye: The lens was dislocated nasally and upward, leaving a rim below, where the zonular fibers were present. Three zones could be distinguished: a narrow, transparent peripheral one; a large, concentric, opaque portion, with clear cortex anteriorly, and a hollowed central area, partially covered with a white, diamond-shaped membrane, attached above and below to the rest of the opacity and leaving at either side a rim, through which the bottom of the central hollow could be seen (fig. 7).

Left Eye: The lens appeared smaller than usual and was dislocated upward and nasally to a greater extent than the lens in the right eye, with a rim of intact zonular fibers. Three portions could also be seen in this lens: a narrow, transparent peripheral zone, a dense, opaque subcortical zone and a large central hollow zone. The last, which was situated very deep, was square with sharply cut edges, formed only by a fairly dense membrane, which became clearer toward

the center. This portion appeared as though a part of the lens had been excised with a sharp instrument. (The inset in figure 7 gives a fair idea of it.)

The fundi were normal.

Operation.—Two discissions were performed in the right eye, both of them with Ziegler's needle. After the first discission, the large amount of debris practically covered the opening made. The second one was more successful, a small opening persisting above the center; however, the central membrane was very tough. A third operation was done: Wecker's scissors were inserted through a keratome incision and the central membrane was cut, and a large clear opening was obtained.

Resulting vision was 20/70 (with a correction of + 11.00 D. sph. ⊂ + 1.00 D. cyl., axis 120).

The left eye had not been operated on as yet.

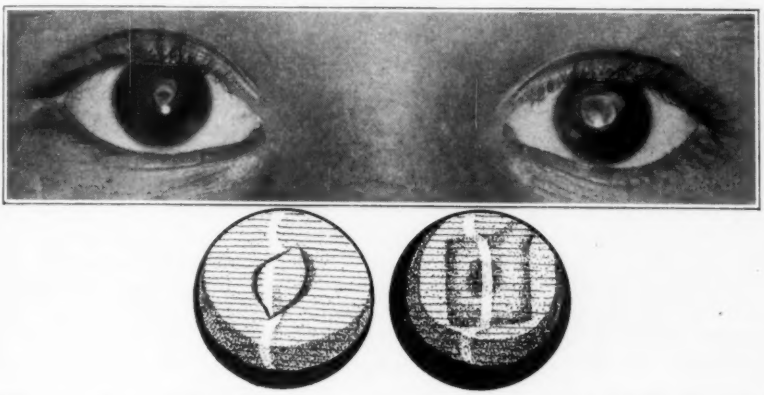

Fig. 7.—Eyes of Nadine L. (III 17). Note the symmetric dislocation of the lenses and their three zones. The center is hollowed and diamond shaped in the right eye and square in the left eye. Surrounding this are a zone of diffuse opacity and a clear periphery. The reflection of the light prevents a clear view of the actual depth of the center.

All these persons, descendants of Grover L. (*II 9*) live at San Jose, Calif. Only 5 of them are clinic patients; the others have been examined at home.

II 10: Sady R., aged 53, the next member of the second generation, was not affected. She was married and had 3 children.

III 18: Pauline R., aged 32, was not affected. She was married and had no children.

III 19: Wilma R., aged 30, was not affected.

III 20: Betty R., aged 21, was not affected. She was married and had no children.

II 11: X. L., a boy, died a few hours after birth.

II 12: X. L., a girl, was stillborn.

II 13: Jessy D., aged 51, had congenital cataracts. She had never had an operation. Vision was very poor; she was barely able to do her housework. She could not read. She was married and had 6 children.

III 21: Paul D., aged 29, had congenital cataracts. He was operated on (two needlings), but the resulting vision was apparently not good. He could not read at all, seeing only well enough "to get around." He was married and had no children.

III 22: Victor D., aged 22, had congenital cataracts. Four discissions were performed, and fairly good vision was obtained. He was able to read and had practically no handicap due to his eyes. He was married and had 1 child.

IV 18: X. D., a boy, 3 months old, was not affected(?).

III 23: Mary D., aged 20, was not affected. She was married and had no children.

III 24: Ruby D., aged 17, was not affected.

III 25: Jessy D., aged 15, was not affected.

III 26: Virgil D., aged 12, was not affected.

These persons, descendents of Mrs. Sady R., live at Buffalo, Mo.

PATHOLOGIC EXAMINATION

The following report was made on the examination of the right eye of Doris D. (IV 11), which was enucleated after a traumatic laceration (Laboratory of Ophthalmic Pathology of the University of California).

"*Gross Examination.*—The specimen consisted of the anterior part of the right eye, previously sectioned through the equator and measuring 23 by 24 by 23 mm.

"There was a scar 5 mm. behind the limbus in the 9 o'clock position. The cornea was clear, showing a widely dilated pupil and a centrally opaque lens. The lens was luxated slightly superiorly, permitting a view into the vitreous between the lower margin of the pupil and the equator of the lens. Viewed from behind, this luxation was more apparent, showing the lower temporal portion of the equator, separated some distance from the ciliary processes. There was, however, no tendency for the lens to 'hinge.' The equatorial diameter was about normal.

"The lens resembled a doughnut, with a central thinned, membranous area, 2.5 to 3 mm. in diameter, which was gray-white. The surrounding ring structure possessed the body of lens substance but showed yellowish opacities extending from the membranous portion toward the equator. The equatorial portion of the lens showed less cataract formation, appearing almost normal."

Microscopic Examination.—The circumcorneal tissues, the cornea, the limbus, the anterior chamber and the iris presented no remarkable features.

". . . The pupillary margin of the upper leaf of the iris was in contact with the lens just ahead of the equator. The lower pupillary border was entirely free of the lens and rested on apparently intact zonular fibers.

"The ciliary body was flattened, especially the coronary portion. The processes were somewhat elongated. Scattered plasma cells were present. Relatively normal and intact, but somewhat elongated, zonular fibers appeared to arise from the valleys both above and below."

The choroid, retina and vitreous were not remarkable.

"Lens: The lens measured about 6 mm. anteroposteriorly at the equator. A central area, 2.5 mm. in diameter, representing the axial portion, was reduced to a membranous band about 0.5 mm. thick, composed anteriorly of an intact folded glass membrane. A wavy glass membrane could be followed along the posterior

surface from each outer margin but appeared to be absent or poorly formed centrally. Enclosed between these two membranes was a groundwork of a pale eosinophilic, slightly fibrillar mass, in which could be found fusiform cells occurring in clumps of three or four or singly, with pale blue nuclei and rather plentiful eosinophilic cytoplasm. Mitoses were not seen, but occasional groups of cells had so little cytoplasmic delineation as to suggest more than a single nucleus per cell. These cells were all separated from each glass membrane. The eosinophilic cytoplasm in places resembled that of normal lens fiber material. Some of this showed vacuolation.

"The doughnut-like portions of the lens measured about 2.5 by 1.5 mm. in diameter above and 2 by 1 mm. below, the shortest measurement being anteroposterior.

"Each fragment was covered by a normal-appearing capsule, with normally arranged epithelial cells anteriorly and normally inserting zonular fibers. The capsule folded together central to the previously described central patch.

"The central portion of the 'doughnut' itself was made up of recognizable lens fibers. The central regions, especially in the upper fragment, showed vacuolation and cataract formation.

"Recently proliferated lens fibers could be traced from equatorial cells and extended beneath the lens capsule. However, most of them terminated blindly with a swollen end adjacent to the anterior epithelium. A definite order was apparent in that the older proliferating fibers lying deeper ended nearer the beginning of the central patch."

SURGICAL TREATMENT OF DISK-SHAPED CATARACT

The surgical treatment of this type of cataract presents another interesting subject. The literature on this aspect of the problem is as yet meager. In my short experience I have found that more than one type of operation is needed, as the cataractous lens is composed of various parts, with distinct structures. A discission exposing the existing lens substance to the solvent action of the aqueous should be the first operation. This also serves as an exploratory procedure in judging the consistency of the membrane, which on occasions can be torn apart or displaced. Collins,[6] in 1 case (that of an 18 month old child), was able to separate the central plaque. In both eyes it fell in the lower part of the anterior chamber and remained there, without any reaction. In most cases the membrane is firmly adherent to the rest of the lens and is too tough to be cut with an ordinary discission needle, so that a stronger instrument must be used. In 2 of our patients (III 17 and IV 11) keratome incisions were made and the central membranes were cut with de Wecker scissors, leaving clear openings in both cases.

Total extraction should be considered with caution. In some cases of this type of cataract the central plaque is adherent to the hyaloid

6. Collins, E. T.: Developmental Deformities of the Crystalline Lens, Ophthalmoscope **6**:577, 1908.

membrane, and extensive loss of vitreous can be produced as in the cases reported by Malbrán and Tosi.[7]

The special characteristics of these cataracts bring up for consideration the advisability of optical iridectomy. The periphery of the lens is clear, so that good visual results may be expected if the eye is otherwise normal. Improvement of vision after sufficient dilation of the pupil should give a hint as to the results to be expected from this operation. If the optical iridectomy proves efficient, it should prevent further surgical trauma, with the familiar picture of a severe reaction. Such a procedure, also, would prevent the inconveniences attendant on aphakia, including the use of strong convex glasses, which are disliked by most children. Fox [2] claimed good results with symmetric nasal iridectomies.

COMMENT

In the family under discussion, consisting of 59 persons, there were 22 males and 37 females. Fifteen of the members were dead; of those remaining, I have a more or less accurate history of 44. Thirteen have been examined. Of the entire 59, 16 are known to have congenital cataracts, but it is not known whether the 3 stillborn infants and the 2 infants who died shortly after birth were affected. Of the 16 members with congenital cataract, 5 were males and 11 females. Two cataractous fathers had 17 children, of whom 6 were affected. Three cataractous mothers had 13 children, of whom 5 were affected. In no case was cataract transmitted from father to son; in 6 cases the condition was transmitted from father to daughter, in 3 cases from mother to son and in 2 cases from mother to daughter. It may be noted that in the second generation the males had affected daughters only, whereas the females had affected sons, although this did not occur in the third generation and it probably happened by chance in the second generation.

So far the descent is direct, except for the first generation, in which neither parent had cataract. No cataract is known to have developed later in life in the unaffected members of this family.

Interesting speculations arise as to the type of heredity in relation to Mendel's laws, even though it is difficult to fit human pedigrees into such laws, especially when they are very short, as was this one. A study of the family tree shows that the transmission has been direct in every instance and that the condition has appeared regularly in the family from the second generation. The members who were not affected had no descendants with cataract. These facts are in favor of a "dominant" type of transmission, but since a dominant character requires

7. Malbrán, J., and Tosi, B.: Catarata anular congénita, Arch. de oftal. de Buenos Aires **15**:543 (Nov.) 1940.

only a single representative to become apparent, one of the parents (in generation I) should have had cataract. However, the presence of the condition in these persons has been denied repeatedly by my informants, and this one fact is against the dominant type of inheritance. If one were to conjecture that this transmission is of the recessive type, one would have to assume that the parents (generation I) were "carriers"; their offspring, however, were affected in a number over the 25 per cent to be expected for the recessive type. Since both of the pair of genes must carry the recessive trait before the characteristic becomes manifest, the affected members must have mated in every instance with persons carrying the same character if the trait were recessive. This is unlikely, especially since no intermarriages have occurred. These facts, as well as the direct and continuous transmission of the defect, are strongly against the recessive type of inheritance. The rule "once free, always free" required by mendelism for a dominant character seems to hold good so far in this degree. Therefore, most of the facts are in favor of a dominant heredity. If the information given about the absence of cataract in the ancestors is reliable, one can regard this defect as a mutation which having once appeared is being transmitted as a dominant. One might surmise that the mutation occurred in the germ line of one parent during an early stage of development.

As to the heredity of the other anomaly present in the eyes examined, that is, the dislocation of the lenses, nothing can be said as yet, since the information on the presence of this condition in other members of the family is practically nil. I have found it in all the cataractous eyes, although this observation must be taken with caution in 2 of the cases (III 8 and III 11) since examination was made after repeated operations, which may have been the cause of the dislocation.

I hope that in the near future I shall be able to examine other members of this family, in order to shed light on several interesting problems. It must also be kept in mind that 8 members of generation III and all of generation IV are young and unmarried; in years to come, therefore, this family tree will probably grow in number and in interest.

From the foregoing observations, it would appear that the germ cell, male or female, is able to transmit to many members of many generations a well defined, and often almost identical, imperfection limited to a small part of the lens. The malign germinal influence, whatever it may be, acts on the lens at an early stage of the fetal development. The range of such influence must be very limited to damage only so small a portion of the body. This is emphasized when one considers that the weight of the normal human lens at 20 to 30 years of age is about 175 mg., or roughly three millionths of the usual body weight at that age.

Descriptions and illustrations of the cataracts found in the present cases place them in the "disk-shaped" type (Collins and Mayou [8]), or "ring" cataract (von Szily [9]). The literature on this type is scanty: In some of the reported cases the condition was discovered on pathologic examination; other cases were studied only clinically, with the exception of von Hess's case, in which the defect was first observed during life and later studied in sections. The first reference seems to be that of Becker (1883) cited by Collins [6] and Malbrán and Tosi.[7] In his "Atlas" Becker described a case with characteristics resembling those of this type of cataract.

Another report is that of Vossius [10] (1893); the cataract in this case was found on pathologic examination in a blind eye with a dense central leukoma preventing clinical study. The eye was enucleated for cosmetic reasons, and the sections showed a cataractous lens with a central opaque portion enclosed between the anterior and the posterior capsule. No nucleus was present.

Collins [11] (1898) described a case of a lens with a central flattened zone in a paper dealing with anterior polar cataracts. At this time, as he admitted in a later paper,[6] he did not realize the significance of the flattened condition of the lens as evidence of lack of development of the nucleus. Such a lens was found in a buphthalmic eye of a 7 year old girl after enucleation. Its condition could not be made out clinically.

The next report was that of von Hess [12] (1905). His patient was first seen when 10 months old and had an iridectomy performed on both eyes. Clinically, there were a dense white central opacity of the lens, with diffuse cloudiness around it, and a clear periphery. The patient died at the age of 17, and Hess obtained the eyes three hours after death. Examination showed flattened, small lenses; in the thickest portion they measured only 2.5 mm, and in the center, 0.5 mm., the shape being similar to that of a red blood cell. The central portion was formed by the anterior and posterior capsules, both of which were wrinkled, with proliferated epithelium between. The

8. Collins, E. T., and Mayou, M. S.: Disc-Shaped Cataract, in Pathology and Bacteriology of the Eye, ed. 2, Philadelphia, P. Blakiston's Sons & Co., 1925, p. 49.

9. von Szily, A.: Ueber angeborene familiäre "Ringstarlinse" nebst Hinweisen auf ihre Entstehung, Klin. Monatsbl. f. Augenh. **81**:145 (Aug. 31) 1928.

10. Vossius, A.: Zur Kasuistik der angeborenen Anomalien des Auges, Beitr. z. Augenh., 1893, no. 9, p. 1.

11. Collins, E. T.: On the Pathogenesis of Anterior Polar Cataract, Tr. Ophth. Soc. U. Kingdom **18**:124, 1897-1898.

12. von Hess: Der Zentralstar: Pathologie und Therapie des Linsensystems, in Graefe, A., and Saemisch, T.: Handbuch der gesamten Augenheilkunde, ed. 3, Leipzig, W. Engelmann, 1911, pt. 2, chap. 9, p. 196.

opacities around the central portion were of the zonular type, and the periphery was clear.

After this case, I was unable to find any further reports until 1928, when von Szily [9] studied a family in which 4 members were affected with this rare type of cataract. The outstanding characteristic of all the lenses examined was, again, the absence of the central portions, which was replaced with an opaque membrane. The lens as a whole was like a ring in every instance. It was noted that the size of the central defect was about the same as the embryonic nucleus.

Another reference may be found in Vogt's [13] "Atlas" (figs. 859 to 861), although the description is not as detailed as the previous ones.

Vázquez Barriére [14] reported a case in 1939 in which the lens was dislocated upward and nasally and was uniformly opaque, with just a few clear blebs. The center was similar to a 2 mm. tunnel and was enclosed by an opaque membrane.

Malbrán and Tosi,[7] in 1940, reported the case of a 14 year old boy whose cataracts were noted shortly after birth. The lenses were dislocated nasally and upward. The authors described the lenses as formed by three portions; a clear peripheral one; a central thin, opaque zone, roughly diamond-shaped, and an intermediate zone between the two, less opaque and thicker than the center, so that the lenses had the form of a life-belt. Both these eyes were operated on. An intracapsular extraction was intended, but the capsule broke. The central zone seemed to be adherent to the hyaloid membrane, which was ruptured by the traction, with loss of vitreous. Pathologic examination of the specimens confirmed the clinical diagnosis of the type of cataract.

As to the type of developmental disturbance, congenital cataract has been considered as due to "arrest" in development, but, as Mann [15] stated, the word "arrest" indicates that normal development has simply been held at some stage without proceeding along abnormal lines, whereas "aberration" means that the resulting structure does not resemble any normal stage; therefore, any congenital opacity must be regarded as an aberration, since the lens is transparent during its normal development.

Various theories have been evolved regarding the embryonic changes leading to this type of cataract.

Vossius [10] interpreted his case as due to a nutritional defect of the axial portion of the lens, secondary to perforation of a corneal ulcer.

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13. Vogt, A.: Atlas der Spaltlampenmikroscopie des lebenden Auges, Berlin, Julius Springer, 1921.

14. Vázquez Barriére, A.: Catarata anular congénita (Ringstarlinse, von Szily), Arch. de oftal. de Buenos Aires **14**:875 (Oct.) 1939.

15. Mann, I.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937, pp. 340 and 359.

Van Hess [12] concluded that this anomaly was probably due to a disturbance in the separation of the lens vesicle, and he classified this cataract as congenital, stationary and "central."

Collins,[6] in his interesting communication on the developmental deformities of the crystalline lens, reviewed the different stages of development in an attempt to place the time and type of disturbance leading to this anomaly. Before the lens vesicle has become completely closed anteriorly, the cells which form the posterior layer elongate and continue to do so after the vesicle is complete, filling its cavity. These are the primary fibers, which later are surrounded by others laid on at the sides and form the nucleus of the lens. If the cells forming the posterior layer for some reason fail to elongate and become transformed into fibers, the nucleus will not be formed, so that the laterally developed fibers will have nothing to encircle. The failure of development of the nucleus does not check the activity of the cells lining the anterior and lateral parts. The central mass results from the proliferation of the cells lining the anterior capsule, probably as an outcome of a low intracapsular pressure. The secondary fibers, having no nucleus to surround, form accumulations at the sides of the anterior mass, with irregularities and vacuolations.

Von Szily,[16] on the basis of his studies of congenital disturbances of the lens, explained the embryology of this type of cataract somewhat differently. The importance of these studies resides in the proof that in all the genuine "idiokinetic" malformations (that is to say, hereditary malformations) "divergence from normal morphology is primary and disintegration of lens substance secondary." The opposite occurs in those forms of cataract in which the opacities affect a lens of normal structure. Injuries of diverse sorts, acting even in the very earliest stages of development, produce a primary distintegration with secondary morphologic disturbance.

On the basis of this theory, von Szily stated that "ring" cataracts can be attributed to a secondary disintegration of the whole thickness of the central portion of the lens, following "idiokinetic" disturbances in the normal delimitation of the two main sections of the embryonic lens, namely, the epithelium and the fibers. The nucleus is resorbed, so that the anterior capsule, together with epithelium, meets the posterior capsule, thus forming the central membrane. The enclosed remains of the lens epithelium is inclined to proliferation, so the membrane may become similar to capsular cataract.

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16. von Szily, A.: (*a*) Kernschwund orden die soz. "Ringstarlinse," in Henke, F., and Lubarsch, O.: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1937, vol. 9, pt. 3, p. 82; (*b*) Doyne Memorial Lecture: Contribution of Pathological Examinations to Elucidation of the Problems of Cataract, Tr. Ophth. Soc. U. Kingdom (pt. 2) **58**:595, 1938.

According to most authors, this malformation is bilateral and hereditary; however, it is admitted that similar pictures may be found as secondary changes of other intraocular processes. Von Szily stated that such changes can be distinguished from typical disk-shaped cataract in that the ring is not always closed and the central membrane contains some fiber material. In the present cases, the presence of bilateral, congenital, hereditary cataract places the lesion with the genuine disk-shaped type, that is, one due to idiokinetic, rather than local ocular, disturbances.

"Ring" cataract may occur in otherwise normal eyes or may be associated with other abnormalities, such as aplasia or hypoplasia of the fovea, an occurrence explaining the poor vision obtained even after a good pupillary opening has been made or after dilation of the pupil, with exposure of the clear margin.

The association of disk-shaped cataract and dislocation of the lens is not infrequent, as can be seen in the description of the cataractous eyes we have examined and in the cases reported by von Szily,[9] Vázquez Barriére[14] and Malbrán and Tosi.[7]

Von Szily[16b] expressed the belief that if the cataract persists for a long time the central defect may become larger, owing to a secondary resorption phenomenon. In 1 of the present cases (II 9) the central portion of the right lens was filled with a flocculent material (as though a discission had been performed). One wonders whether this could be explained by the resorption phenomenon just mentioned.

Regarding the other anomaly found in the reported cases, namely, the dislocated lenses, it can in all probability be designated as "ectopia lentis," as it has all the characteristics described for this condition: congenital, hereditary, bilateral and symmetric. The displacement in these cases belongs also to the most common type, that is, upward and nasally.

Although ectopia lentis as a rule has a distinct hereditary tendency, sporadic cases have been described by Bell (cited by Mann[15]) and even cases of unilateral occurrence, by Parsons (cited by Mann[15]). It may occur exclusively in females or males but usually has no sex predominance.

From its hereditary and bilateral character, ectopia falls into a different group than coloboma despite the fact that irregularities and notches can be found in the edges of the ectopic lens. The zonule, however, is not so often absent in ectopia as in coloboma. The defect seems to be due to actual dislocation rather than to failure of development. The embryologic features of this condition are not well established as yet. When it appears as an isolated character, there is no evidence of primary abnormality of any structure but the zonule. It

appears to have no connection with coloboma or persistence of capsulopupillary vessels. It is probably an irregularity in the length and strength of the fibers, which causes the lens to be pulled toward the strongest ones. Since the dislocation occurs most commonly upward, weakening of the inferior zonular fibers is revealed. Regarding this fact Mann [15] stated: "If the zonule fibers are going to fail, they are more likely to do so in the lower part, which (being the unstable region of the fissure) is always most likely to show underdevelopment."

This explanation regards ectopia lentis as due to a defect limited to ectodermal structures, but the fact that anomalies of the iris, such as corectopia, polycoria and persistent pupillary membrane, are found in pedigrees showing ectopia cannot be overlooked. In 2 members of the reported family (III 16 and IV 14) I have found persistent pupillary membranes as an isolated character.

SUMMARY

A family of 59 members, representing four generations, is reported on. Sixteen of them had congenital cataracts. There were no known cases of this condition in the generations preceding the four reported on here.

All the members examined presented the type of cataract known as "disk-shaped," or "ring," characterized by the absence of the lens nucleus. This is due either to a failure of development of the primary fibers (Collins) or to a secondary resorption of the central parts, following an idiokinetic disturbance at an early stage (von Szily). This suggests the presence of genes controlling the development of the nucleus. Apparently, such genes are dominant.

Association of these cataracts with ectopia lentis was found in all the patients examined. No other local or systemic anomaly was present.

Members of the Department of Ophthalmology, Stanford University School of Medicine, and of the Laboratory of Ophthalmic Pathology, University of California Medical School, gave help in the preparation of this paper.

Correspondence

REVIEW OF AN OLD BOOK: CONSERVATION OF VISION, J. G. A. CHEVALLIER, PARIS, 1812

To the Editor.—The author, Chevallier, was not a physician but a civil engineer. He seems to have known quite a bit about optics but was mostly interested in the practical side of his craft. In those days glasses were not prescribed by physicians, and he was probably the first reputable and learned optician to practice in Paris. He always had an eye to commerce and often blew his own horn, a characteristic which may be justified when one compares him with his colleagues of that day.

The second half of the book is of no great interest to ophthalmologists. It gives a description of various optical instruments, such as telescopes, mirrors and microscopes. The first half deals with the eye and with glasses. There is nothing one can learn today in these two hundred pages; but, as is often the case in old books, one finds amusing things—and now and then one is surprised by an accurate statement.

First comes a short chapter on the anatomy of the eye, then a rapid survey of the pathology of the eye. This book, being meant for the lay public, and the eventual purchaser of glasses, is written neither by nor for the medical profession; but it makes amusing reading, and this work of vulgarization is not bad.

Chevallier states, for instance, that squint should be treated early and advises occlusion against the amblyopia of squint. Strangely enough, he states that the oblique muscles are the real cause of strabismus.

The author mentions that cataract is often found among persons engaged in occupations in which they constantly face a strong fire, and this clinical remark reminds one of the injurious effect ascribed at present to infra-red rays. He is less fortunate in stating that cataract can be the cause of the central scotoma.

There are some interesting pages on the first contact with the outside world of patients operated on late in life for congenital cataract. These observations are similar to those made in more recent times, i. e., that the patient must control his new sensation by touch and that at first everything seems to be very near, and almost in contact with his eyes.

There is a fairly good description of keratoconus, but extraction of the lens is advocated.

Chevallier mentions the importance of a correct pupillary distance for glasses, but, of course, not because of any esophoria or exophoria. What he stresses is that one should look only through the center of a lens, as the periphery shows aberration.

He mentions Wollaston's periscopic lenses and understands clearly their qualities. However, he seems mostly to have manufactured bispherical lenses. Bifocal lenses of the Franklin type were known to him.

Blue glasses are rightly considered as "cool."

There is some general good advice on the hygiene of the eye; for example, one is pleased and surprised to read that one (in 1820) should sleep with an open window to have more air.

It would be interesting to know how he chose the glasses for his patients, but he does not go into that. It seems to have been a sort of Donders method, by trial, starting from a chart, which he prints, giving the most usual glasses for a given age. (He evidently dealt especially with presbyopia, although he also gave concave lenses for myopia. Cylinders were, of course, unknown to him).

Much of his optical business was done by mail. He usually sent three pairs of glasses, and the patient chose the best.

Chevallier ground his own glasses and tells how.

EDWARD HARTMANN, Paris, France.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Summer Graduate Course in Ophthalmology, University of Rochester School of Medicine and Dentistry.—The Fourteenth Summer Graduate Course in Ophthalmology, under the auspices of the University of Rochester School of Medicine and Dentistry, will be held on August 5, 6, 7 and 8, 1946.

The subjects of lectures and guest speakers follow: "Differential Diagnosis of Paralysis of Vertically Acting Muscles" and "Clinical Problems," Dr. Francis H. Adler; "Anomalies of the Fundus" and "The Fundus in Myopia," Dr. Arthur J. Bedell; "Slit Lamp Microscopy," Dr. Harvey E. Thorpe; "The Measurement of Strabismus" and "The Management of Strabismus in Children," Dr. Maynard C. Wheeler; "Herpes Simplex Cornea," "Herpes Zoster Cornea," "Experiences with Unusual Corneal Diseases" and "Ophthalmologic Problems Met at Morocco," Dr. Trygve Gunderson; "Physiologic Optics in Refraction," Mr. Frederick W. Jobe; "Everyday Spectacle Problems," Mr. Irving Lueck; "Ophthalmic Surgery," Dr. J. S. Guyton; "External Diseases of the Eye" and "The Management of Dacryocystitis," Dr. Ralph O. Rychener; "Ophthalmic Research in the Navy," Alexander E. MacDonald. On the final day there will be a surgical clinic at the Strong Memorial Hospital and a visit to the Bausch & Lomb factory.

Training Course at Rochester Orthoptic Center.—The Rochester (N. Y.) Orthoptic Center is receiving applications for its next training course for orthoptic technicians. This course is accredited by the American Orthoptic Council. Information may be received from the Rochester Orthoptic Center, 208 North Goodman Street, Rochester 7, N. Y.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Cornea and Sclera

TREATMENT OF SEPTIC ULCER OF THE CORNEA BY LOCAL APPLICATIONS OF PENICILLIN. F. JULER and M. Y. YOUNG, Brit. J. OPHTH. **29:** 312 (June) 1945.

No attempt was made in this series to evaluate the effect of intramuscular administration of penicillin. The product was applied by local methods only.

The number of ulcers treated was 23, 2 of which occurred in the same eye, with an interval of one month between their appearances. The ages of the patients affected were distributed as follows:

Seven were over 60 years of age; of these, 4 did excellently, and 3 did well. Seven were between 50 and 60 years of age; 1 did badly, 3 did excellently and 2 did poorly. Seven were between 40 and 49 years of age; 2 did well and 5 excellently. One was 35 years of age and did not react to penicillin—the infecting organism was Bacillus pyocyaneus. One was 14 years of age and reacted excellently.

The solution used was sodium penicillate in a strength of 500 units per cubic centimeter. Two drops of the solution was instilled in the lower conjunctiva or, if possible, on the cornea itself. After several seconds the instillation was repeated. This procedure was carried out hourly by day and every two hours by night until the condition was obviously under control, when longer intervals were permitted. Atropine sulfate was used three or four times daily. The Saemisch section is advocated in cases of serious lesions. W. ZENTMAYER.

General

OPHTHALMIC WORK IN A BRITISH GENERAL HOSPITAL IN NORTH AFRICA. A. J. CAMERON, Brit. J. Ophth. **29:** 26 (Jan.) 1945.

This interesting article does not lend itself to satisfactory abstraction. The nature of the cases is described, and a number of unusual injuries, including foreign bodies in the eye, the orbit and the adnexa, are described. A large percentage of intraocular foreign bodies were nonmagnetic. Mortar fragments were preeminently the cause of wounds.

The opinion is expressed that myopic persons in subtropical countries tend with a definitely less strong lens to get as good vision as they previously had and that men with low myopia who required a correction to obtain vision of 6/9 or better could read 6/6 easily without correction. The author offers no scientific explanation of this observation but thinks the reason might be partly that the bright light produces a smaller pupil or that these men had become accustomed to gazing into the wide open spaces and leading an outdoor life. W. ZENTMAYER.

General Diseases

PERIARTERITIS NODOSA AFFECTING THE EYE. R. SAMPSON, Brit. J. Ophth. **29:** 282 (June) 1945.

An airman aged 20 years was admitted to a hospital with generalized clonic convulsions, followed by unconsciousness lasting several hours. Increasing anemia and emaciation with failure of the left ventricle resulted in death, after an illness of three months. Pathologic examination demonstrated well marked periarteritis affecting arteries in all systems, particularly the coronary arteries. Ophthalmoscopic examination made four weeks before death showed in the right eye retinal vessels of normal caliber and generalized retinal edema, more marked on the temporal half of the fundus, with blurred margins of the disk. Lateral to and above the level of the macula were several areas of retinal detachment of small extent, and deep to the retina in these areas were grayish white, branching nodules, somewhat resembling miliary tubercles of the choroid. In the left eye there was a large globular, exudative detachment of the retina, with no holes or tears. A week before death the fundi looked normal except that there were small, lightly pigmented scars at the sites of the choroidal lesions previously noted. No sign of albuminuric retinopathy was present. The eyes and the orbital contents were obtained for examination. The main interest lies in the presence of healed arteritis in many of the choroidal vessels. Similar appearances were in evidence in the retinal vessels in the disk of the right eye and in some of the extrascleral vessels.

W. ZENTMAYER.

Injuries

SURGICAL APPROACH IN TREATMENT OF PENETRATING INJURIES OF SCLERA IN REGION OF CILIARY BODY. J. KOPP, Vestnik oftal. **23:** 18, 1944.

Kopp gives a thorough analysis of his vast experience in treating injuries of the region of the ciliary body in both civilian and military cases.

In cases of injuries of the ciliary body the important factor is the secondary infection; the most painstaking care of the wound is therefore imperative.

The anesthesia should be adequate. No speculum should be employed, and sutures of the lid should be used instead; sometimes it is necessary to place sutures on some of the rectus muscles. If the patient is seen soon after the injury, the prolapsed vitreous is cut off, and the prolapsed ciliary body is put back in place. If the patient is seen a few days after the injury, the prolapsed ciliary body should be excised. Sometimes the ciliary body is pressed back with a spatula while the scleral sutures are being tied. Kopp applies scleral sutures in cases of gaping wounds only, while in cases in which the scleral edges are in apposition he uses conjunctival sutures.

In 11 cases of penetrating injuries of the ciliary body with intraocular foreign bodies, one eye was lost because of iridocyclitis and another because of purulent infection. The foreign bodies were extracted by the diascleral method according to the localization of the

foreign body. In 19 cases of penetrating injuries of the sclera and ciliary body without intraocular foreign bodies, 10 eyes had to be eviscerated because of panophthalmitis, and 2 had to be enucleated because of iridocyclitis. In the remaining 7 cases the results were as good as with any injury of the eye.

Analysis of 30 cases of penetrating injuries of the region of the ciliary body in wartime shows that the same approach can be used as in management of industrial traumas. In 12 of these cases there were exudates in the vitreous but only 4 eyes had to be enucleated. In 18 cases the prolapsed ciliary body was excised and scleral sutures were applied; only 4 eyes had to be removed because of severe iridocyclitis. Most of these patients came under observation several day after the injury.

Kopp concludes that injuries of the region of the ciliary body should be treated with all possible speed and that most of the eyes can be saved if seen shortly after the injury. O. SITCHEVSKA.

PURULENT MENINGITIS AND DEATH FOLLOWING AN OCULAR INJURY: REPORT OF A CASE. L. ZATZ, Vestnik oftal. **23**: 47, 1944.

A soldier received an injury of the left eye from a fragment of a mine. The eye was enucleated at a front line hospital, and recovery was uneventful; but after a time meningeal signs appeared: rigidity of the neck, a bilateral Kernig sign and absence of knee reflexes. The spinal fluid showed the picture of purulent meningitis. Sulfanilamide was given intravenously and intraspinally, but despite this therapy the patient died. Autopsy showed a blind penetrating injury of the skull, the basal bone and the frontal lobe of the brain; there were abscess of the frontal lobe, basal purulent meningitis and an intracranial foreign body measuring 12 by 8 mm.

Zatz therefore makes a plea for a routine roentgenographic examination in cases of crushing injuries of the eye, as well as a neurologic study, in order to avoid such a tragic result. O. SITCHEVSKA.

Lacrimal Apparatus

"DACRYORHINOPLASTY." A. BLERAS GARCIA, Arch. Soc. oftal. hispano-am. **4**: 26 (Jan.-Feb.) 1944.

When the operation of dacryocystorhinostomy fails or is not suitable, either of two new procedures can be made use of: Arruga's operation (canaliculorhinostomy) and the operation of "dacryorhinostomy." The latter operation is in some respects like the one described by the author: dacryorhinoplasty. In 80 per cent of 200 cases in which Casanellos used the new technic the operation was successful. Bleras Garcia, without knowledge of the work of Casanellos, was at the same time experimenting on the cadaver with the same procedure. Three cases in which he performed the operation, with good results in 2, are reported.

Mucous membrane from the lip was used for the graft. Two quadrilateral grafts were cut; one was sutured to the posterior border of incisions in the conjunctival mucous membrane, and the other, to

the anterior border. In this way a passage from the lacus lacrimalis to the interior of the nose was established. The technic of the operation is described in detail. This procedure was successful in the human subject.

H. F. CARRASQUILLO.

Neurology

VISUAL DISTURBANCES PRODUCED BY BILATERAL LESIONS OF THE OCCIPITAL LOBES WITH CENTRAL SCOTOMAS. M. B. BENDER and L. T. FURLOW, Arch. Neurol. & Psychiat. **53:** 165 (March) 1945.

The authors report in detail a case of bilateral lesion of the occipital lobe, describing and discussing the clinical picture from the time of injury throughout the period of recovery. After the patient had been completely amaurotic, vision returned in the peripheral fields, and restitution continued to take place medially, terminating in bilateral large central scotomas. During the period of recovery he had good perception of motion, defective color vision, little appreciation of form and ability to see best in the dark or in low illumination, all visual functions characteristic of the peripheral portions of the retina (in this case the peripheral "cortical retina").

The patient also manifested (*a*) the normal mechanism of psychologic filling in of visual field defects, thus perceiving objects as a whole; (*b*) retention of his psychologic field of vision about a subjective central point in a blind area, which made it difficult for him to realize that his central vision was lost; (*c*) reorganization of his psychologic field of vision when a new functional fovea was formed; (*d*) entopic phenomena, with visualization of emanating "waves," and (*e*) fluctuation of perception in the remaining field of vision.

Opticomotor nystagmus was induced by having a striped drum revolve in his peripheral, but not in his central, fields of vision. Five months after the injury after-imagery could not be elicited with a light stimulus placed in any part of the field of vision.

S. R. IRVINE.

HEMIFACIAL SPASM: REVIEW OF ONE HUNDRED AND SIX CASES. G. EHNI and H. WOLTMAN, Arch. Neurol. & Psychiat. **53:** 205 (March) 1945.

The records of 663 patients seen at the Mayo Clinic for various unwonted movements of the face were reviewed by the authors; of these, 106 had cryptogenic hemofacial spasm. The report excludes cases in which there was evidence of a gross pathologic lesion in the posterior fossa or the peripheral course of the facial nerve.

The following conclusions are drawn:

1. Women are more often afflicted than men, in the ratio of about 6 to 4.

2. Children do not have hemifacial spasm.

3. Encephalitic illnesses or arteriosclerosis, with or without hypertension, seldom bears a causal relation to hemifacial spasm.

4. The spasms usually begin in the orbicular oculi muscle on one side and slowly progress to adjacent muscles until, in certain cases, the entire facial musculature is involved.

For 7 patients the authors have no definite information as to the exact location of onset of the twitching. In all but 9 of the remaining 99 patients the muscles of the eyelids were involved early. Sixty-nine patients described their spasm as beginning in the eyelids; 7 patients in the upper lid, and 18 patients, in the lower lid alone, while in 21 patients the involvement ranged from the eyelids and "quivering in the ear drum" to twitching of the whole side of the face. The reason for the high incidence of early involvement of the lids is not known. Gowers explained the proneness to spasm in the orbicularis oculi muscle by saying that the "motor mechanism of this muscle is more sensitive, in consequence of its energetic reflex action." Oppenheim and other authors accepted this explanation without modification. In 9 of the patients the spasms did not start in the eyelids, and in 2 of these persons the lids never became involved.

5. Spontaneous remissions for periods up to three years have been noted.

6. The spasms in almost every case were aggravated by circumstances causing nervousness, fatigue or voluntary movements of the face.

7. No patient was able to stop the spasm by an exercise of the will.

8. Only 5 patients were seemingly cured without resort to surgical treatment, and in 3 of these the disturbance may well be in a period of remission.

9. Spinofacial anastomosis was performed on 3 patients, with satisfactory results in all.

10. There is evidence for the view that the lesion causing this condition is in the facial nucleus or the proximal portion of the facial nerve.

S. R. IRVINE.

SYNKINETIC PUPILLARY PHENOMENA AND THE ARGYLL ROBERTSON PUPIL. M. D. BENDER, Arch. Neurol. & Psychiat. **53:** 418 (June) 1945.

The author describes a case of skull fracture and complete paralysis of the right oculomotor nerve following a fall. The case is one of oculomotor ophthalmoplegia from which there was rapid but incomplete recovery, with iridoparesis and associated synkinetic phenomena as residua. On contraction of any of the formerly paralytic extraocular muscles, especially the inferior rectus, the sphincter of the right pupil contracted simultaneously. If this pupil were examined only for the conventional reactions to light and in convergence, the clinical picture would simulate the Argyll Robertson pupil. Another interesting feature of this case was the synkinetic contraction of the ciliary muscle in association with action of any of the formerly ophthalmoplegic muscles.

A second case is reviewed in which skull fracture was followed by blindness of the left eye, inability to raise either eyelid and paralysis of all movements in both eyes except abduction of the right eye. This case is another instance of recovery from oculomotor ophthalmoplegia with residual paralysis to stimulation with light and synkinetic constriction of the pupils. Were it not for the pupillary contractions associated with ocular movement other than convergence, the clinical

picture would strongly simulate the syndrome described by Argyll Robertson. It is interesting and significant that in this case, and in the preceding case, practically all the formerly paralyzed external ocular muscles recovered. Only the sphincter pupillae remained paretic, being inactive to light but contracting in association with movements of the eyes.

A third case is reported with signs of paralysis of the third, fourth and fifth canial nerves on the left side. The causative factor was syphilis. After improvement with treatment, the left pupil would have been classified as the Argyll Robertson type were it not for the synkinetic phenomena, apparent not only in the sphincter pupillae but also in the superior eyelid. The retraction of the eyelid in association with ocular movements has been called the pseudo-Graefe phenomenon.

The details of 4 animal experiments are given. The phenomena of synkinetic pupillary constriction and retraction of the eyelid were produced experimentally in the monkey by intracranial section of the oculomotor nerve. These phenomena are partly explained by the theory of indiscriminate regeneration of oculomotor nerve fibers. It is concluded that the so-called, or pseudo, Argyll Robertson pupil, sometimes noted after head injury with complicating oculomotor ophthalmoplegia, has no etiologic relationship to the classic pupillary reaction originally described by Argyll Robertson.

S. R. IRVINE.

BRANCH THROMBOSIS OF MIDDLE CEREBRAL ARTERY. K. C. WYBAR, Brit. J. Ophth. **29:** 355 (July) 1945.

A middle-aged woman suddenly experienced left-sided headache associated with a defect of the right side of both visual fields. There was transient aphasia of the receptive type with disturbance of comprehension of written speech and with a slight jargon aphasia.

The visual agnosia, which is the only persistent feature, is a right superior homonymous quadrantic scotoma adjacent to the fixation point with sharply defined vertical and horizontal borders. The peripheral border, which was at first vague, is now more decided. There is incongruity between the scotomas, the left one being larger than the right.

The clinical picture is in agreement with a diagnosis of thrombosis of the parietotemporal branch of the left middle cerebral artery.

W. ZENTMAYER.

Ocular Muscles

HEREDITY AS A FACTOR IN SQUINT. L. P. DARR, Am. J. Ophth. **28:** 898 (Aug.) 1945.

Darr refers to various authorities and concludes that heredity may be a factor in squint and that it should be watched for in families in which it has occurred.

W. S. REESE.

DIVERGENCE PARALYSIS AND HEAD TRAUMA. N. SAVITSKY and M. J. MADONICK, Arch. Neurol. & Psychiat. **53:** 135 (Feb.) 1945.

The authors report 6 cases of divergence paralysis encountered in a series of 1,550 personally observed cases of head injury. Only

5 similar instances were found among 17,783 cases of head injury reviewed in the literature, perhaps because the patients are often too ill to be tested or because careful examinations are not made to determine its presence. The authors are of the opinion that there is insufficient proof that this condition can occur on a hysterical basis and that the head trauma causes injury to the hypothetic center for divergence in the midbrain. In some cases the complaint persisted so long (up to five years after injury) that the lesion could be considered irreversible, perhaps a laceration.

S. R. IRVINE.

Trachoma

TRACHOMA IN WEST AFRICAN NEGROES. J. G. SCOTT, Brit. J. Ophth. **29:** 244 (May) 1945.

The purpose of the paper is to assess the rate of infection among Negroes in British West Africa and to describe the disease as it affects the natives.

Trachoma of the West Coast African Negro is a mild disease. It is of the general infiltrative type. It affects 5 per cent of school children, 10 per cent of soldiers and 25 per cent of population in some villages in the Gambia. The same disease is found in 10 per cent of soldiers on the Gold Coast, in 10 per cent of Nigerian soldiers and in 2 per cent of Cameroon soldiers. Three hundred American Negro soldiers had no similar infection but were not immune.

W. ZENTMAYER.

Tumors

MALIGNANT PALPEBRAL TUMORS. PEREZ-BUFIL, Arch. Soc. oftal. hispano-am. **4:** 59 (Jan.-Feb.) 1944.

Early surgical removal of malignant palpebral tumors and covering of the gap with lateral flaps are advocated by the author. He considers this treatment preferable to roentgenotherapy. Five cases are reported in which good results were obtained with respect to cure and cosmetic effects.

H. F. CARRASQUILLO.

CHOLESTEATOMA OF THE ORBIT. J. BASTERRA, Arch. Soc. oftal. hispano-am. **4:** 67 (Jan.-Feb.) 1944.

The author reports a case of this rare condition, only 8 cases of which are recorded in the literature. The patient, a woman aged 49, complained of protrusion of the left eye. A tumor about the size of a cherry was observed between the upper orbital brim and the eyeball. The tumor was removed, and pathologic examination revealed "small masses formed by cellular detritus undergoing lipid degeneration."

A discussion of this tumor is given.

H. F. CARRASQUILLO.

RECURRENT GLIOMA OF THE RETINA TREATED BY CHAOUL'S METHOD OF ROENTGEN IRRADIATION. C. COSTA, Arch. Soc. oftal. hispano-am. **4:** 72 (Jan.-Feb.) 1944.

The left eye of a boy 1 year old was enucleated for a glioma. Five months later the tumor recurred in the orbit. Treatment was with

irradiation according to the method of Chaoul. This technic is considered better than the ordinary method of roentgen irradiation. One month later the tumor had disappeared entirely. Three months later, however, the growth reappeared. The child is still under treatment.

H. F. CARRASQUILLO.

Vitreous

SURGICAL TREATMENT OF HEMOPHTHALMOS. KAMINSKAYA, Vestnik oftal. **23:** 3, 1944

Kaminskaya treated surgically 25 patients with hemorrhages into the vitreous according to Nedden's method. The treatment consisted in withdrawal of from 0.2 to 0.6 cc. of vitreous by puncturing the sclera at a point 5 to 6 mm. below and temporal to the limbus. This procedure could be repeated two or three times at intervals of six weeks. No reaction was observed. Hypotony of the eye was observed for several days, but usually the tension became normal ofterward. Vision was increased to a considerable degree in a few patients. Kaminskaya recommends this method as the most effective and at the same time the simplest. It was particularly useful in treatment of wartime victims of intraocular hemorrhages due to injuries.

O. SITCHEVSKA.

Therapeutics

INJECTION OF SULFONAMIDE COMPOUNDS INTO THE ANTERIOR CHAMBER. J. L. CASTILLO, Arch. de oftal. de Buenos Aires **19:** 81 (Feb.) 1944.

Although the concentration of sulfanilamide in the blood may be high, it is always lower in the intraocular tissues and fluids. With the idea of bringing to a higher level the concentration of this drug in the eye, the author introduced a 5 per cent solution directly into the anterior chamber after removal of the aqueous humor. The tolerance of the 4 patients subjected to the experiment was very good. The author suggests this method of administration for a more active and shorter course of therapy in cases of infectious processes of the cornea, anterior chamber and uvea.

H. F. CARRASQUILLO.

LOCAL USE OF SULFONAMIDE COMPOUNDS FOR OCULAR DISEASES. E. SELFA, Arch. Soc. oftal. hispano-am. **3:** 442 (Nov.-Dec.) 1943.

The sulfonamide compounds may be used systemically or locally. For local use the author has used advantageously a 5 per cent solution of sodium sulfapyridine, 5 and 10 per cent solutions of sulfathiazole and a 5 to 25 per cent solution of sulfamethylthiazole. The drugs have been used locally with good results in treatment of acute pseudomembranous conjunctivitis occurring with whooping cough; phlyctenular conjunctivitis; gonococcic ophthalmia neonatorum, inclusion conjunctivitis of the newborn, and acute conjunctivitis produced by the staphylococcus, the Koch-Weeks bacillus or the pneumococcus, as well as in the conservative treatment of stricture of the lacrimal passages and as an application to the lids after operations for ectropion and trichiasis.

H. F. CARRASQUILLO.

Society Transactions

EDITED BY DR. W. L. BENEDICT

SECOND PAN-AMERICAN CONGRESS OF OPHTHALMOLOGY

Conrad Berens, M.D., New York

Preliminary Report of Meeting at Montevideo, Uruguay, Nov. 26-Dec. 1, 1945

Our Uruguayan colleagues were royal hosts to the Second Pan-American Congress of Ophthalmology, which was held in Montevideo. It was encouraging to see such a splendid gathering of ophthalmologists of the Western Hemisphere so shortly after the cessation of international hostilities. Dr. Vasquez Barrière, of Montevideo, president of the congress, opened the meeting, stressing inter-American cooperation for the advancement of ophthalmology and the prevention of blindness. He then presented a most illuminating history of ophthalmology in the Americas. In conclusion, Dr. Vasquez Barrière stated that he was sure that this meeting of the Pan-American Congress of Ophthalmology marked a new stage in the ophthalmology of the Americas. He reminded those present of the great work of Dr. Harry Gradle in establishing the Pan-American Congress of Ophthalmology and expressed deep regret that Dr. Gradle was not able to be present.

This was a great loss to the meeting, and Dr. Gradle's constructive presidential address was read by Prof. Moacyr Alvaro, of Brazil. Dr. Gradle wrote:

"This, the second meeting of the Pan-American Congress of Ophthalmology, marks an important epoch in the history of ophthalmology in the Americas. For two years this meeting has been postponed, not only because of travel conditions imposed by the war but even more because of the handicaps on science that unleashed brutality produces. But now we can gather in quiet and peace to describe and discuss how best we, the ophthalmologists of the Western Hemisphere, may aid our people. It is solely for that purpose that the Pan-American Congress of Ophthalmology exists.

"But a forum of this character must be more than merely a meeting place for the exchange of scientific ideas. To be of real value to all its members, there must be constructive aspects that will tend to advance the science of ophthalmology in all parts of the world inhabited by members of the Congress. The constructive phase of the society cannot be confined to the time of the meetings alone but must live with the members day by day. It must be a power, a force, the sole object of which is the advancement of the science of ophthalmology and to which the members can turn as necessary. Your officers of the Pan-American Congress of Ophthalmology are endeavoring to supply that force through *Ophthalmología Ibero Americana,* through the Kellogg Pan-American fellowships in ophthalmology and through the work of

the various committees, whose reports you are to hear within the next few days.

"Through practical experience in the United States of America and in Brazil, it has been found that the most potent factor in the elevation of the standards of ophthalmology is the existence of a board for the purpose of setting standards and for the voluntary examination of men who wish to be recognized by their fellows as qualified in ophthalmology. To that end, I propose the development of a South American Board of Ophthalmology, dedicated to the elevation of the standards of training and of the practice of ophthalmology. Such a board should, of course, be an independent institution, originated by the educators in ophthalmology and supported by all the local and national ophthalmologic societies. Each country should be represented by elected representatives in the proportion of 1 to each hundred ophthalmologists in the country. The board should meet once a year and should determine which of the applicants from all the countries are eligible for examination. Then the examination should be determined on, and on his return home the examination should be given in each country by the elected representative, assisted by as many oculists as he may deem necessary. Only those candidates approved by the general board should be eligible for the examination. On successful completion of the examination, a certificate should be granted by the board, and eventually such certificate should be required for appointment to hospital or university positions.

"It is one of the greatest regrets of my life that I am unable to be with you for this meeting in person, but my thoughts and my hopes will be with you constantly. May your labors prove interesting and valuable, and may the fruits of your labors bring advancement in knowledge to world ophthalmology."

Dr. Gradle's recommendation to form a board of ophthalmology for Latin America was later acted on and accepted.

Among the North American ophthalmologists who were present were: Dr. Thomas D. Allen, of Chicago; Capt. Clifford A. Swanson, representing the United States Navy; Comdr. Walter P. Griffy, representing the United States Public Health Service; Dr. Joseph I. Pascal, of New York; Dr. Ramón Castroviejo, representing the American Ophthalmological Society; Dr. Conrad Berens, representing the American College of Surgeons, and Dr. Paul Tisher, of New Britain, Conn.

The meeting offered an excellent opportunity to hear of the splendid work done in South America in the treatment of ocular diseases and in the prevention of blindness. Mrs. Merrill, the executive director of the National Society for the Prevention of Blindness, was hostess at a luncheon for representatives of all the countries participating in the congress. The progress in preventing blindness was described by each of the representatives.

One of the highlights of the meeting was Dr. Arruga's arrival from Spain. It was unfortunate that his trip was delayed by storms, but it was stimulating to have him present even for a part of the meeting. His discussion of the treatment of detachment of the retina was based on his recent experiences and was a most valuable contribution to knowledge of this subject.

One of the important resolutions passed at the meeting was to change the name of the organization to the Pan-American Association of Ophthalmology. The officers of the association, elected at the Montevideo meeting, were as follows: president, Dr. Harry S. Gradle; honorary president, Prof. Alberto Vasquez Barrière; vice presidents, Dr. Francisco Belgeri (Argentina), Dr. Frank Brawley (United States of America), Dr. J. Pereira Gomes (Brazil), Dr. Frederick C. Cordes (United States of America), Dr. J. A. MacMillan (Canada), Dr. Alexis Aguero (Costa Rica), Dr. C. Espildora Luque (Chile), Dr. R. Pacheco Luna (Guatemala) and Dr. A. Torres Estrada (Mexico); executive secretaries, Prof. Moacyr E. Alvaro (Brazil) and Dr. Conrad Berens (United States of America). Communications concerning the association should be addressed to Prof. Moacyr E. Alvaro (1151 Rua Consolação, São Paulo, Brasil), if mailed south of Panama, and to Dr. Conrad Berens (301 East Fourteenth Street, New York 3), if mailed north of Panama.

The committee on ophthalmologic education appointed a president, Dr. Jorge Valdeavellano (Lima, Peru), and three secretaries, whose work will be divided as follows: Dr. Thomas D. Allen (Chicago), in charge of Canada and the United States; Dr. Miguel Branly (Cuba), in charge of Mexico, the continental countries of Central America, the Islands of the Caribbean, Venezuela and Colombia, and Dr. Raul Rodriguez Barrios (Montevideo, Uruguay), in charge of Ecuador, Peru, Boliva, Chile, Argentina, Paraguay and Brazil.

The committee on Kellogg fellowships appointed Dr. Harry S. Gradle, Dr. Conrad Berens, Dr. Tomas Yanes and Prof. Moacyr E. Alvaro to represent the association.

The committee appointed to draw up a constitution and by-laws for the association consist of Dr. Tomas Yanes, Dr. Conrad Berens and Prof. Alberto Vazquez Barrière.

The scientific program was most instructive, and the proceedings will be published in a later issue of the ARCHIVES.

The next meeting of the association is planned for February 1948 in Habana, Cuba. Ophthalmologists in the Western Hemisphere will soon receive a communication inviting them to become members of the association and to participate in the work of this organization. Membership includes a subscription to the association's official publication *Ophthalmologia Ibero Americana.*

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Warren S. Reese, M.D., *Chairman*

George F. J. Kelly, M.D., *Secretary*

Dec. 20, 1945

Amblyopia Due to Dietary Deficiency: Report of Eight Cases. COMMANDER A. D. BEAM, U.S.N.R. (by invitation).

Early in the spring of 1944 the United States Naval Hospital in Philadelphia was designated by the Surgeon General as the national center for the rehabilitation of blinded personnel of the Navy and the

Marine Corps. Only men whose vision with correction is 20/200 or less in the better eye are admitted to this special service. Up to the time of this report, 165 patients have been admitted. Of these, 101 had suffered loss of vision as a result of traumatic injury; 29, as a result of methyl alcohol poisoning, and 27, after various ocular diseases. The remaining 8 patients became blinded during their period of imprisonment under the Japanese. It is this last group of patients with whom I am concerned in this report.

All 8 men, with normal vision on enlistment, were captured at the fall of Corregidor. Five of them were Marines and 3 sailors, only 1 of whom had sustained physical injury during the encounter prior to capture, and that was confined to the lower extremities. They were all between the ages of 20 and 32 years. Before capitulation, for five months, their living conditions had been far from satisfactory, and their diet had been rationed and steadily reduced. After capture all 8 men survived the death march from Bilibid to Cabanatuan, where 6 of them were imprisoned until the date of liberation, on Feb. 4, 1945. The remaining 2 were later taken to Japan, after they had begun to have visual deficiency. During their period of imprisonment all of them were forced to engage in strenuous physical labor and suffered the physical hardships of discipline now so well known to every one. Loss of weight varied from 40 to 60 pounds (18 and 27 Kg.) among the 8 men. The diet during the entire period of incarceration was far below that specified by international law. The average daily intake was 200 to 300 Gm. of polished rice, or about 7 tablespoons, and a thin soup made with sweet potato vine, which was given about three times a week. This constituted a diet of approximately 1,000 calories per day. Occasionally the intake was greater or less, but this represents the usual food intake. All these patients showed evidence of severe beriberi, and 7 of them had pellagra, of varying degrees of intensity. Visual loss appeared in all of them, without other specific prodromes, and proceeded to the maximum deficiency in one to four weeks. Blindness in all these prisoners developed between four and one half to eight months after capture. Once the loss of sight was established, it remained static, even after they were freed and given various forms of therapy. Loss of vision was painless in each instance, and except for the signs of dietary insufficiency there were no common factors that would suggest a toxic, infectious or traumatic cause. In addition, 7 of the patients had bilateral nerve deafness, in which the hearing loss varied from 11 to 36 decibels. Deafness was a concomitant feature of visual loss and was first noted at the onset of blindness or later. All the 8 men had some evidence of peripheral neuritis, as did nearly all the other prisoners. None of these men had symptoms of night blindness but, on the contrary, found that their vision was better during twilight or early evening. Hypoproteinemia and occasional bouts of diarrhea were common to all the prisoners, including those under discussion. All these patients stated that there were many other prisoners who became blind in a similar manner but failed to survive the period of confinement for one reason or another.

These 8 men with severely impaired vision present histories and physical signs which indicate that their visual loss probably resulted from dietary deficiency. However, the possible effect of some chemical

intoxication cannot be completely disregarded, even though there does not seem to be any common factor. The effect of a prolonged deficiency in diet on the visual sense of man during a period of strenuous and enforced labor has never been determined. Therefore, there may have been three groups of etiologic factors: deficiencies in such required elements as vitamins, minerals and proteins; intoxications of a chemical and bacterial nature, and the effect of strenuous physical activity with inadequate caloric intake. I am unable to state just what influence each of these factors had on the development of blindness in the circumstances just related, but from the endless array of published data it would appear that avitaminosis is the principal factor to consider. However, in discussing vitamin deficiencies, I do not intend to exclude the possible effects of other contributing factors or to indicate any assessment of their influence.

Only the vitamins usually thought to be concerned with the physiology of the eye will be considered, vitamin D being excluded.

Vitamin A.—The minimum daily requirement of vitamin A is considered to be about 5,000 international units. The source of vitamin A in the diet of these men was limited to that contained in the thin soup made from vegetable leaves and water. None of these men suffered from night blindness, and only 2 showed evidence of corneal disease on admission to this hospital. One patient had had a perforating corneal ulcer in his right eye, whereas there were no opacities or history of inflammation of the left eye. On examination at this hospital, the lower two thirds of the cornea of the right eye was opaque and vascularized, and there was an anterior synechia. The left eye showed proliferation of the limbic vessels. One other patient had had "sore eyes" three months after capture. An American physician told him that he had corneal ulcers; these lesions became symptomless with no change in diet and with treatment limited to instillation of yellow mercuric oxide once a day. When this man was first examined here, there were seven or eight superficial opacities of each cornea associated with well marked proliferation of the limbic vessels. The corneal opacities were not dense, and there was little loss of corneal substance. These 2 cases may represent keratomalacia and xerosis of the cornea, respectively, although in neither was there evidence of conjunctival xerosis nor had the patients suffered from day blindness.

Thiamine.—Thiamine, or vitamin B_1, has been proved necessary in maintaining normal neurologic function. Inadequate ingestion, absorption or utilization of this heat-labile portion of the vitamin B complex causes the disease known as beriberi. The Committee on Nutrition of the National Research Council recommends between 1.5 and 2 mg. daily for a well balanced diet.

The rice which these men ate was chiefly polished. The polishing process, like the milling of flour, removes valuable constituents, notably the vitamins, protein and mineral elements. The discovery that a diet which consists solely of polished rice will produce beriberi gave an early incentive to the study of vitamins. Polished rice is practically devoid of all vitamins, but beriberi is due specifically to the lack of thiamine.

Each man in this group suffered symptoms of severe beriberi, including peripheral neuritis, edema of the extremities, weakness, anorexia

and diarrhea. Palpitation and shortness of breath were noticed by 3 of them. Massive doses of thiamine hydrochloride, given on their liberation in 1945, relieved all these symptoms; but the amblyopia which had occurred during the attack of beriberi was not improved. One patient received large doses of vitamin B complex seven months after his vision failed, when the Japanese selected a group of 100 prisoners all suffering from beriberi, half of whom were given vitamin therapy in addition to the usual diet, while the other half was maintained on the unfortified rice and soup diet. This man improved during this study with respect to his neuritis, edema and weakness; however, there was no change in his vision during or after the six weeks of the experiment.

On their admission to this service, the vision of these 8 men ranged from 1/200 to 10/200 in the better eye. Each had bilateral absolute central scotoma, which extended 5 to 12 degrees from the fixation point, and 2 also had bilateral concentric contraction of the peripheral fields. The pupils were semidilated and reacted sluggishly to light. The results of funduscopic examination were essentially normal except that each man showed evidence of bilateral atrophy of the optic nerve, varying from well marked temporal pallor to advanced atrophy. The atrophy was of the primary, or descending, type. Treatment, consisting of a high vitamin diet supported by large doses of thiamine hydrochloride, has failed to cause any visual improvement in these patients. There is considerable evidence in the literature to support the theory that lack of thiamine in the diet may cause retrobulbar neuritis and optic nerve atrophy if the condition remains untreated. The dietary deficiency associated with chronic alcoholism is a classic example.

Nicotinic Acid.—Pellagra is a disease of nutrition caused by deficiency in nicotinic acid (the P-P factor). Although other factors of the vitamin B complex may contribute to this disease, their significance is uncertain. Typical cases of pellagra are characterized by three groups of symptoms: a typical form of dermatitis, digestive disorders with or without diarrhea and psychoses of the confusional type. Typical signs of this disease occurred in 7 of the 8 patients presented here. The other patient apparently had no evidence of pellagra, even to the extent of glossitis, which is often one of the first signs of nicotinic acid deficiency. Although peripheral neuritis and atrophy of the optic nerve have been attributed to this disease (Wilkinson), it is probable that concomitant thiamine deficiency is the true etiologic factor. The occurrence of atrophy of the optic nerve and peripheral neuritis in the patient who presented no signs or symptoms of pellagra tends to support this belief. These men suffered no ocular change which it is thought can be directly attributed to nicotinic acid deficiency. Their pellagra healed soon after their liberation, when they received large doses of vitamin B complex.

Riboflavin.—In 1940 Sydenstricker described the ocular effects of a riboflavin deficiency which included the symptoms of photophobia, sensations of roughness or burning of the eyelids and visual fatigue. The commonest sign was circumcorneal injection, often with invasion of the cornea by capillaries from the limbic plexus. Superficial corneal nebulas were also noted. These signs and symptoms responded favor-

ably to riboflavin therapy. Four men in this group gave a history of having had "sore eyes" and photophobia during their period of incarceration. Three of the 4 men exhibited definite proliferation of limbic vessels, and 1 showed superficial corneal opacities on examination here. The remaining men showed no evidence of proliferation of the limbic capillaries. Local areas of proliferation, usually traceable to an antecedent corneal inflammation, were not considered. Symptoms of photophobia and burning were relieved soon after liberation, when adequate vitamin therapy was instituted, but no change in the vascular proliferation has been noted during the past eight to ten weeks. A daily dose of 5 mg. of riboflavin has been administered daily since the patients arrived here.

Vitmin C.—The ocular manifestations of vitamin C deficiency are probably limited to ocular hemorrhage in patients with scurvy. However, there is some evidence that cataract formation may be influenced by lack of this vitamin in the diet. Three of these patients were told that they had scurvy at one time or another while prisoners on Luzon. Their description of the cutaneous lesions is not typical, although their gums were swollen and bled easily. They gave no history of subcutaneous hemorrhage or bleeding except from the gums and nose. Examination here revealed no pathologic condition of the eyes attributable to vitamin C deficiency.

Comment.—In this group of 8 men who became amblyopic while on an inadequate diet during imprisonment the outstanding pathologic change in the eyes common to all of them was the atrophy of the optic nerve, with central scotoma in each eye. Dietary deficiency, notably in thiamine, appears to have been the etiologic factor. Signs and symptoms of severe beriberi were present in each case, thus establishing proof of thiamine deficiency. Analysis of the diet, the bulk of which was polished rice, reveals little or no source of this vitamin. Rice contains 79.4 per cent carbohydrate, 7.6 per cent proteins and 0.3 per cent fat, which gave them a high carbohydrate diet. It has been well established that the thiamine requirement increases with the carbohydrate intake and with physical exertion. Ten hours of hard labor per day associated with a high carbohydrate diet increased the thiamine requirement. The need for thiamine was great and the source negligible. There is lack of evidence to support the influence of other avitaminoses on the amblyopia from which these patients suffer.

Again, no attempt has been made to evaluate the significance of other possible contributing factors due to dietary deficiency, intoxication or circumstances of existence such as were endured by these men. Only in highly controlled circumstances could such a study be of definite value. Certainly, these variable factors cannot be assessed in retrospect.

DISCUSSION

DR. WALTER I. LILLIE: Commander Beam has presented a series of patients with typical chronic retrobulbar neuritis and resulting simple atrophy of the optic nerve due to deficiency of the vitamin B complex in the diet. The patients were sailors and Marines who were prisoners of the Japanese. He has definitely shown that the condition was actually due to a deficiency of thiamine. I have seen similar cases at Valley Forge Military Hospital, in the Army personnel; so one can conclude

that all branches of the service under similar conditions are similarly affected. One of the sailors noticed that while he was on the polished rice diet his vision diminished but when he was fed the unpolished rice his vision improved. He always made an effort to obtain as much unpolished rice as possible.

In the treatment of these debilitated states due to dietary insufficiency, one must be careful in giving dextrose intravenously. If it is not fortified with vitamin B, it will utilize the remaining vitamin B in the body tissues and produce an added deleterious effect.

Method of Closing the Cataract Incision by Sliding a Large Conjunctival Flap from Above Down over a Corneoscleral Suture.

Dr. P. H. Decker, Williamsport, Pa. (by invitation).

This conjunctival flap will temporarily bury the corneoscleral suture and the entire incision. About the fourth or fifth day the conjunctival sutures spontaneously cut out, allowing the conjunctival flap to retract, thus automatically exposing the corneoscleral suture, which is removed about the tenth day.

The principle behind this procedure is that the corneoscleral suture gives adequate strength to closure of the incision, preventing loss of vitreous, while the conjunctival flap has an adequate sealing effect on the closure, allowing rapid and early reformation of the anterior chamber. By combining the two procedures, namely, the corneoscleral suture and the large sliding conjunctival flap, both needed elements in closure of the incision are obtained, that is, loss of vitreous is guarded against by the corneoscleral suture and delayed reformation of the anterior chamber, with its complications, is prevented by the conjunctival flap.

A film showing the operative procedure in 6 cases was presented.

DISCUSSION

Dr. William Zentmayer: In looking up the literature for Dr. Decker, I found that this procedure had been employed by Kuhnt in cataract operations.

Kuhnt makes a large conjunctival flap, as described by Dr. Decker; in addition he makes a horizontal incision well up in the cul-de-sac. The latter allows for greater freedom in bringing down the flap and, therefore, better coverage of the wound than can be obtained without that incision.

Dr. Edmund B. Spaeth: I had the pleasure of seeing Dr. Decker's film with him at his home; so he knows, at least in part, what I am about to say, for we had a discussion at that time. It seems to me that he lays too much stress on the necessity for firm closure. His two lateral sutures with the sliding conjunctival flap will give this in all but extraordinary circumstances. At the same time the conjunctival flap should seal off the anterior chamber.

I agree with him as to the necessity of closing the anterior chamber promptly. For years I have used the conjunctival flap for closure in all cataract operations in one-eyed patients. Nonformation of the anterior chamber, if it continues for more than two or three days, can cause serious consequences. His beautiful film shows that without any possibility of difference of opinion, in a most conclusive manner.

Dr. James S. Shipman: I also should like to congratulate Dr. Decker on this beautiful presentation of an interesting subject. From

the pictures that he has shown I cannot see the necessity for using any suture. The way in which the cataracts were delivered and the way in which he kept his patient's eyes so still was beautiful to see. I should like to ask what kind of anesthesia he used. Every cataract operation that was shown was done skilfully and with little trauma. Certainly, so far as could be seen from the picture, there was no danger of immediate loss of vitreous.

The only excuse for a suture in this operation would be for his second reason, that of preventing delayed closure of the anterior chamber. In his technic, excellent as it was, I did not once see where he replaced the iris pillars. What happens to them? Was the pupil dilated with atropine or with homatropine? What drug was instilled at the first dressing? Was it atropine? To me these points are important and have a great deal to do with the closure of the anterior chamber. In my opinion, if the pillars are not replaced, they will be incarcerated to a certain degree and will lead to slow closure of the anterior chamber. I still believe that there is no necessity for using atropine for the first dressing when good intracapsular extraction has been performed, as was done in all these cases. Atropine is necessary in doing an extracapsular extraction, in which a good deal is involved, but with a complete intracapsular extraction there is no necessity for it. Certainly, there is no need of employing atropine until the anterior chamber has reformed, and it is my experience that the majority of them do reform within twenty-four to forty-eight hours after operation. A large conjunctival flap is a great help in getting the anterior chamber to reform, and it eliminates one of the objections to cataract extraction without a suture, i. e., slow closure of the anterior chamber.

I have not come to believe that sutures are necessary for safe cataract extraction. I can do a better operation without them, and I do not use them except on rare occasions. I used one last week in an eye in which I knew there was vitreous in the wound, as the result of a basal iridectomy. The man was a poor patient, and I did not have his facial nerve blocked. Later, I had to remove the lens, and I felt that vitreous would present itself when I made the section. I enlarged the iridectomy incision slightly, then inserted three corneoscleral sutures before completing the section; but, in spite of this, vitreous is still seeping from the wound, ten days after extraction. I cannot be convinced that corneoscleral sutures or conjunctival sutures, such as Dr. Spaeth described, will keep the vitreous in when it is going to escape. If vitreous is going to be lost, it will be, regardless of any suture. I still feel that a well made corneal section with a good conjunctival flap is the best operation for cataract extraction.

DR. P. H. DECKER: I wish to thank Dr. Shipman for his comments, but I still feel that sutures are necessary, at least in my hands. With regard to replacing the iris pillars, this is always done when there is any question of incarceration. I omitted this step in order to conserve film; however, I might add that I do not always insert an instrument into the anterior chamber after the extraction in order to replace an imaginary incarceration, as I feel that there is danger of inadvertently rupturing the hyaloid membrane with any unnecessary intraocular instrumentation after the extraction of the lens.

Book Reviews

Physical Chemistry of Cells and Tissues. By Rudolf Höber, M.D., with the collaboration of David I. Hitchcock, J. B. Bateman, David R. Goddard and Wallace O. Fenn. Price, $9. Pp. 676, with 70 illustrations. Philadelphia: The Blakiston Company, 1945.

Those who knew R. Höber's standard work on the physical chemistry of cells and tissues looked forward with great expectation to the first edition in English. This work has had six German editions between 1902 and 1926 and has been frequently called the bible of the physicochemistry of cells. The expectations are amply fulfilled by the English edition, which is by no means a condensation of the former publications but is an entirely new book, which covers the recent developments in the field of cellular physicochemistry. In the introduction, selected principles of physical chemistry are presented by D. L. Hitchcock in a concise and clear form, similar to that of his book, "Physical Chemistry for Students of Biology and Medicine" (Springfield, Ill., Charles C Thomas, Publisher, 1940). This part is supplemented by a comprehensive section by J. B. Bateman on the physicochemical properties of large molecules (micellae, films, membranes) and their architectural and functional significance in living matter.

The main subject of cellular physiology, by Höber, is contained in the subsequent six sections. They deal with the architecture of protoplasm; the surface of the protoplast, its properties and architecture, and the influence of some extracellular factors on cellular activity and on passive penetration and active transfer in animal and plant tissues. This part of the work includes a section on respiration of cells and tissues, by D. R. Goddard, and another on contractility, by W. O. Fenn. The limitation of the final six sections to about 400 pages and the neglect of several recent physicochemical aspects of physiology were necessitated by war conditions, as Höber states in the preface. Nevertheless, an incredible amount of information and valuable references will be found in these pages.

There is scarcely a problem in ophthalmology whose study would not be benefited by the basic and broad information contained in Höber's book—whether on permeability, penetration and active transfer, respiration of tissues or the basic principles of physical chemistry. Höber's hope that the text may be a "guide to new roads into the unknown" applies also to research in ophthalmology. This book should be an integral part of the library in any biologic laboratory.

LUDWIG VON SALLMANN.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.
Place: Habana, Cuba. Time: February 1948.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. D. S. Shen, Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, Szechuan, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

Faculty of Ophthalmologists

President: Brig. Sir Stewart Duke-Elder, 63 Harley St., London, W. 1, England.
Secretary: Mr. Frank W. Law, 45 Lincoln's Inn Fields, London, W. C. 2, England.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Mr. E. F. Wilson, 24 Upper Northgate St., Chester.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield 3.
Place: Manchester, Leeds, Newcastle-upon-Tyne, Liverpool, Sheffield and Bradford, in rotation. Time: October to May.

Ophthalmological Society of Australia

President: Dr. J. Ringland Anderson, Astor House, 108 Collins St., Melbourne, Victoria.
Secretary: Dr. D. A. Williams, 27 Commonwealth St., Sydney.
Place: Melbourne. Time: Oct. 20-26, 1946.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of Hospital de Nuestra Señora de la Luz

Chairman: Dr. Manuel J. Icaza y Dublán, México, D. F., Mexico.
Secretary: Dr. Jorge Meyrán, México, D. F., Mexico.

Ophthalmological Society of South Africa

President: Dr. A. W. Sichel, National Mutual Bldg., Church Square, Cape Town.
Secretary: Dr. J. K. de Kock, Groote Kerk Bldg., 32 Parliament St., Cape Town.

Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.
Place: London. Time: May 30-June 1-2, 1946.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Time: July 4-6, 1946.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

Royal Society of Medicine, Section of Ophthalmology

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

São Paulo Society of Ophthalmology

President: Silvio de Almeida Toledo, Barão de Ilapetininga St., 88, 5° Andar, São Paulo, Brazil.
Secretary: Dr. Plinio de Toledo Piza, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

Scottish Ophthalmological Club

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

Sociedad Argentina de Oftalmologia

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

Sociedad Oftalmologia del Litoral, Rosario (Argentina)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Arturo Etchemendigaray, Villa Constitución, Santa Fé.
Place: Rosario. Time: Last Saturday of every month, April to November. All correspondence should be addressed to the President.

Sociedade de Oftalmología del Norte

President: Dr. Alberto Cárdenas.
Secretary: Dr. Jorge Luis Castillo, Mendoza 421, Tucumán, Argentina.

Sociedade de Oftalmologia de Minas Gerais

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

Sociedade de Oftalmologia e Otorrinolaringologia de Rio Grande do Sul

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4, III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.
Place: Palmer House, Chicago. Time: Oct. 13-18, 1946.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. Eugene M. Blake, 303 Whitney Ave., New Haven, Conn.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.
Place: San Francisco. Time: June 26-28, 1946.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto 5.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto 5.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Walter W. Wright, 170 St. George St., Toronto 5.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.
Place: New York. Time: Nov. 25-27, 1946.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. Anthony Ambrose, 31 Lincoln Park, Newark.
Secretary: Dr. William F. Keim Jr., 15 Washington St., Newark 2.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Stuart Broadwell, 101½ N. 5th St., Springfield, Ill.
Secretary-Treasurer: Dr. William F. Hubble, 861-867 Citizens Bldg., Decatur, Ill.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. P. G. Spelbring, 131 S. Barstow St., Eau Claire.
Secretary: Dr. G. L. McCormick, 650 S. Central Ave., Marshfield.

HAWAII EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. F. J. Pinkerton, 7 Young Hotel Bldg., Honolulu.
Secretary-Treasurer: Dr. L. Q. Pang, 52 S. Vineyard St., Honolulu 39.
Place: Honolulu. Time: Third Thursday of each month.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Howard F. Hill, 177 Main St., Waterville, Maine.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston 16.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Julius A. Weber, 640 Stimson Bldg., Seattle 1, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1, Wash.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, Sterling, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. A. R. McKinney, 330 S. Washington St., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

Sioux Valley Eye and Ear Academy

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

Southwestern Michigan Triological Society

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. Ray Parker, 218 Franklin St., Johnstown, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit National Bank Bldg., Dubois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. E. C. Moulton, 619 Garrison Ave., Fort Smith.
Secretary: Dr. K. W. Cosgrove, 7 Urquhart Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. George H. Stine, 23 E. Pikes Peak Ave., Colorado Springs.
Secretary: Dr. J. Leonard Swigert, 320 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. Paul B. MacCready, 442 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 666 Cherry St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. E. Stewart, 721 Wabash Ave., Terre Haute.
Secretary: Dr. Russell A. Sage, 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. S. A. O'Brien, 1 N. Federal Ave., Mason City.

Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. B. Granger, Emporia.
Secretary: Dr. George F. Gsell, 911 Beacon Bldg., Wichita 2.

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. George S. Adkins, 121 N. President St., Jackson, Miss.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, SECTION ON EYE, EAR, NOSE AND THROAT DISEASES

Chairman: Dr. William T. Hunt Jr., 1205 Spruce St., Philadelphia 7.
Secretary: Dr. Gabriel Tucker, 250 S. 18th St., Philadelphia 3.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Edmond L. Cooper, 1553 Woodward Ave., Detroit 26.
Secretary: Dr. Ralph H. Gilbert, 110 Fulton St. E., Grand Rapids.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Karl C. Wold, 1051 Lowry Bldg., St. Paul 2.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul 2.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. H. Casebeer, 44 W. Park Ave., Butte.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. C. W. Buvinger, 50 Washington St., East Orange.
Secretary: Dr. Z. Laurence Griesemer, 1145 E. Jersey St., Elizabeth.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.
Secretary: Dr. Thomas H. Johnson, 30 W. 59th St., New York.

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. A. J. Ellington, 412 S. Spring St., Burlington.
Secretary: Dr. J. A. Harrill, Bowman Gray School of Medicine, Winston-Salem.
Place: Hendersonville. Time: Sept. 16-19, 1946.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. E. D. Perrin, 221–5th St., Bismarck.
Secretary-Treasurer: Dr. M. T. Lampert, Minot.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Wilfred Belnap, 833 S. W. 11th Ave., Portland.
Secretary-Treasurer: Dr. C. W. Kuhn, 1020 S. W. Taylor St., Portland 5.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

PENNSYLVANIA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Thomas F. Furlong Jr., 36 Parking Plaza, Ardmore.
Secretary: Dr. Benjamin F. Souders, 143 N. 6th St., Reading.
Time: Last week in April.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. J. H. Stokes, 125 W. Cheves St., Florence.
Secretary-Treasurer: Dr. Roderick Macdonald, 330 E. Main St., Rock Hill.
Place: Hendersonville, N. C. Time: Sept. 16-19, 1946.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George Burchfield, Maryville.
Secretary-Treasurer: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. E. B. Fairbanks, 315 Medical Arts Bldg., Salt Lake City.
Secretary-Treasurer: Dr. Dean Spear, 516 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Thomas E. Hughes, 1000 W. Grace St., Richmond.
Secretary-Treasurer: Dr. Francis H. McGovern, 105 S. Union St., Danville.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Secretary: Dr. Lester A. Brown, 815 Doctors Bldg., Atlanta, Ga.
Place: Academy of Medicine. Time: 7:30 p. m., fourth Monday of each month from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Jonas Friedenwald, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Fred Reese, 330 N. Charles St., Baltimore 1.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. W. Chunn Parsons, 425 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.
Secretary-Treasurer: Dr. Louis Freimark, 256 Rochester Ave., Brooklyn 13.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. William H. Howard, 389 Linwood Ave., Buffalo 9.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo 9.
Time: Second Thursday of each month from October to May.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago 2.
Secretary: Dr. J. R. Fitzgerald, 3215 W. North Ave., Chicago.
Place: Continental Hotel, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. M. Paul Motto, Rose Bldg., Cleveland.
Secretary: Dr. H. H. Wygand, 624 Guardian Bldg., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. Burton Chance, 317 S. 15th St., Philadelphia.
Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. M. Goldberg, 328 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. W. J. Miller, 21 E. State St., Columbus, Ohio.
Place: University Club. Time: 6:15 p. m., first Monday of each month, from October to May, inclusive.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. F. B. Kelly, 519 Medical Professional Bldg., Corpus Christi, Texas.
Time: 6:30 p. m., third Tuesday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Speight Jenkins, 1719 Pacific Ave., Dallas, Texas.
Secretary: Dr. L. Darrough, Dallas Medical and Surgical Clinics, Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. I. McPherrin, 406–6th Ave., Des Moines, Iowa.
Secretary-Treasurer: Dr. C. C. Jones, Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., fourth Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Wesley G. Reid, 974 Fisher Bldg., Detroit 2.
Place: Club rooms of Wayne County Medical Society. Time: First Monday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Bruce Fralick, 201 S. Main St., Ann Arbor, Mich.
Secretary: Dr. William S. Gonne, 619 David Whitney Bldg., Detroit 26.
Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. Frank C. Furlong, 713 Union St., Schenectady.
Secretary-Treasurer: Dr. E. Martin Freund, 762 Madison Ave., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. C. R. Lees, 602 W. 10th St., Fort Worth 2, Texas.
Secretary-Treasurer: Dr. Van D. Rathgeber, 1305 Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. J. Matt Robison, 1304 Walker Ave., Houston, Texas.
Secretary: Dr. John H. Barrett, 1304 Walker Ave., Houston, Texas.
Place: River Oaks Country Club. Time: 6:30 p. m., second Thursday of each month from October to June.

Indianapolis Ophthalmological and Otolaryngological Society

President: Dr. J. Jerome Littell, 603 Hume Mansur Bldg., Indianapolis.
Secretary: Dr. J. Lawrence Sims, 303 Hume Mansur Bldg., Indianapolis.
Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.
Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.
Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Francis Carl Hertzog, 117 E. 8th St., Long Beach, Calif.
Secretary-Treasurer: Dr. Robert G. Thornburgh, 117 E. 8th St., Long Beach, Calif.
Place: Seaside Hospital. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. A. R. Robbins, 1930 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. K. C. Brandenburg, 110 Pine Ave., Long Beach 2, Calif.
Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:30 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.
Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.
Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.
Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.
Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.
Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville 3, Tenn.
Place: James Robertson Hotel. Time: 6:30 p. m., third Monday of each month from October to May.

New Orleans Ophthalmological and Otolaryngological Society

President Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Brittain F. Payne, 17 E. 72d St., New York 21.
Secretary: Dr. Milton Berliner, 57 W. 57th St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Benjamin Friedman, 6 W. 77th St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York 28.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. S. R. Shaver, 117 N. Broadway, Oklahoma City.
Secretary: Dr. William Mussil, Medical Arts Bldg., Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. A. A. Steinberg, 1502 Farnam St., Omaha.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha 2.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clifton Ave., Clifton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. L. Waller Winckler, Philadelphia.
Secretary: Dr. Robert T. M. Donnelly, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Clarence F. Bernatz, Park Bldg., Pittsburgh.
Secretary: Dr. Robert J. Billings, Park Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. Claude W. Bankes, 212 N. 6th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Eye, Ear, Nose and Throat Society

President: Dr. Luther C. Brawner, Professional Bldg., Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. A. Lange, 3903a Olive St., St. Louis.
Secretary: Dr. William Kleinberg, Frisco Bldg., St. Louis.
Place: Oscar Johnson Institute. Time: Fourth Friday of each month from October to April, inclusive, except December, at 8:00 p. m.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. C. B. Cowan, 490 Post St., San Francisco.
Secretary: Dr. D. Harrington, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey, 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. W. W. Randolph, 1838 Parkwood Ave., Toledo 2, Ohio.
Secretary: Dr. John L. Roberts, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

TORONTO ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. R. G. C. Kelly, 14 Lynwood Ave., Toronto 5, Canada.
Secretary: Dr. Alfred Elliott, 802 Medical Arts Bldg., Toronto 5, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

WASHINGTON, D. C., OPHTHALMOLOGICAL SOCIETY

President: Dr. Harold M. Downey, 1740 M St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Richard W. Wilkinson, 1408 L St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

WILKES-BARRE OPHTHALMOLOGICAL SOCIETY

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.